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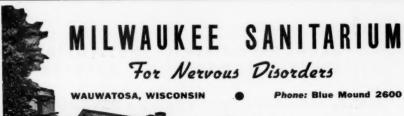
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MECHANISM AND CORTICAL REPRESENTATION OF THE FEEDING PATTERN

B. P. BABKIN, M.D.†

J. M. VAN BUREN, M.D.
MONTREAL, CANADA

BECAUSE of its accessibility and the myriad responses induced by its stimulation, the cerebral cortex has intrigued many investigators since Fritsch and Hitzig ¹ demonstrated its electrical excitability, in 1870. Spencer's ² careful work, published in 1894, showed that autonomic, as well as somatic, functions were represented at the cortical level. Since the work of these pioneers much has been added to our knowledge, and this knowledge has increasingly been applied to clinical problems. The present paper is a summary of the results of a series of experiments on dogs, presented with the hope that it may serve as a guide to a better understanding of the mechanism of action of the human cerebral cortex in relation to autonomic functions.

The term "feeding pattern" is intended to imply the actions of the most rostral part of the digestive tract during the ingestion of food. Specifically, our observations dealt with tongue and jaw movements; salivation; the pharyngeal, laryngeal and esophageal phases of deglutition, and the motor responses of the stomach.³ These effects were produced by stimulation of the anterior portion of the sigmoid gyrus (area A, Fig. 7) and the anterior composite gyrus (areas B, C and D, Fig. 7) of the dog. In order that these effects may be transferred even tentatively to man, brief mention of the comparative anatomy of the region must be made. Consideration of a number of factors leads one to compare the anterior composite gyrus of the dog with the human anterior insular region and the superior bank of the Sylvian fissure at the inferior termination of the precentral gyrus.⁴

[†]Prof. Babkin died May 3, 1950.

From the Department of Neurology and Neurosurgery, McGill University, and the Montreal Neurological Institute.

^{1.} Fritsch and Hitzig, 1870; cited by Ferrier, D.: The Functions of the Brain, London, Smith, Elder & Co., 1876.

Spencer, W. G.: The Effect on Respiration by Faradic Excitation of the Cerebrum in the Monkey, Dog, Cat, and Rabbit, Phil. Tr. Roy. Soc. London 185:609-662, 1894.

^{3.} In addition, some 30 acute experiments were carried out under identical conditions in an attempt to induce gastric secretion by cortical stimulation in the sigmoid and anterior composite gyrus regions. Negative results were obtained.

^{4. (}a) Ariëns Kappers, C. U.; Huber, G. C., and Crosby, E. C.: The Comparative Anatomy of the Nervous System of Vertebrates, Including Man, New York, The Macmillan Company,

In Figure 1 Penfield and Rasmussen's data derived from stimulation of the human cerebral cortex are compared with those of the present experiments on dogs. In the dog, jaw indicates opening of the mouth, and when this response was seen the area of stimulation lay above that of the more complicated act of mastication. In man the area for simpler jaw movements also lay above that for mastication, and in about half of these the response consisted of opening the mouth. Of the remainder, some at least were lateral deviations of the mandible, which the dog is not anatomically equipped to duplicate. In the dog mastication was combined with deglutition, salivation and inhibition of gastric peristalsis as the complicated response of a single cortical point to stimulation. Data on man, however, showed the combination of mastication and salivation, but throat movements (swallowing and gagging) were not noted. Penfield and Rasmussen reported the occasional production of abdominal sensation on stimulation of the anterior insular region and suggested that this might be an expression of a motor response of the gastrointestinal tract. The only effect apparent on stimulation of the canine cortex was inhibition of gastric peristalsis, but the use of general anesthesia in our experiments may be responsible for the apparent contradiction in results.

At the outset, we wished to follow by our recording methods the movements of the most proximal portion of the gastrointestinal tract during deglutition induced by a variety of means, some, perhaps, approximating normal stimuli in character. Therefore, the first group of experiments dealt with swallowing induced by stimulation of the afferent nerves of the pharynx, larynx, esophagus, and stomach. From this work it was hoped that some general principles might be observed which would lend themselves to a better understanding of events following stimulation of the cerebral cortex. The experiments on the cerebral cortex formed the second part of our study.

Since the response of these regions to cortical stimulation has been frequently observed over the years in both man and animals, our interest was centered primarily on the coordination and organization of these responses. As work progressed, the spatial intermingling of cortical autonomic and somatic representation became increasingly apparent, as did the fact that functions elicited by cortical stimulation appeared not to be elaborated at that level but, rather, to receive their character and organization in the brain stem.

SUMMARY OF LITERATURE

Experiments dealing with the initiation of deglutition by stimulation of afferent nerves date well back into the past century. Palugyay 5 credited Bidder and

^{1936. (}b) Klempin: Über die Architektonik der Groshirnrinde des Hundes, J. f. Psychol. u. Neurol. 26:229-249, 1921. (c) von Economo, C.: The Cytoarchitectonics of the Human Cerebral Cortex, London, Oxford University Press, 1929. (d) Ferrier, D.: The Functions of the Brain, London, Smith, Elder & Co., 1876. (e) Garol, H. W.: The "Motor" Cortex of the Cat, J. Neuropath. & Exper. Neurol. 1:139-145, 1942. (f) Woolsey, C. N., and Fairman, D.: Contralateral, Ipsilateral, and Bilateral Representation of Cutaneous Receptors in Somatic Areas I and II of the Cerebral Cortex of Pig, Sheep and Other Mammals, Surgery 19:684-702, 1946. (g) Penfield, W., and Rasmussen, T.: The Cerebral Cortex of Man, New York, The Macmillan Company, 1950.

^{5.} Palugyay, J.: Schlucken, Handb. norm. u. path. Physiol. 3:348, 1927.

Blumber with being the first to observe, in 1865, that swallowing movements followed stimulation of the central end of the superior laryngeal nerve. Deglutition following mechanical stimulation of the posterior pharyngeal wall was studied in anesthetized animals by Meltzer ⁶ and Kahn. ⁷ Burget and Zeller ⁸ observed that relaxation of the cardiac sphincter followed spontaneous swallowing and esophageal distention in dogs with chronic esophageal fistulas. A predominantly inhibitory effect on gastric motility or tone following deglutition, oronasal and afferent vagal stimulation has been reported by various authors. ⁹

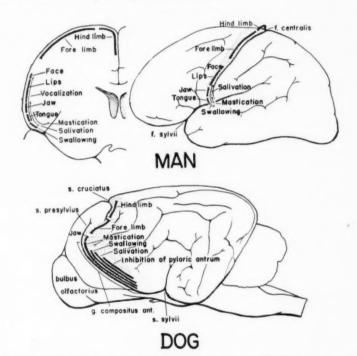


Fig. 1.—Diagram illustrating the distribution of the motor representation in man and dog. The area containing "motor cortex" defined as thick agranular cortex with giant pyramidal cells in the fifth layer has been indicated in dots. Adapted from Penfield and Rasmussen, 48 Klempin, 40 and von Economo. 4c

Meltzer, S. J.: On the Causes of the Orderly Progress of the Peristaltic Movements in the Oesophagus, Am. J. Physiol. 2:266-272, 1898.

Kahn, R. H.: Studien über den Schluckreflex: I. Die sensible Innervation, Arch. f. Anat. u. Physiol., Supp., pp. 386-426, 1903.

^{8.} Burget, G. E., and Zeller, W. E.: A Study of the Cardia in Unanesthetized Dogs, Proc. Soc. Exper. Biol. & Med. 34:433-434, 1936.

^{9.} Morat, J. P.: Sur quelques particularitiés de l'innervation motrice de l'estomac et de l'intestin, Arch. de physiol. norm. et path. 5:142-153, 1893. May, W. P.: The Innervation of the Sphincters and Musculature of the Stomach, J. Physiol. 31:260-271, 1904. Auer, J.: Gastric

In the cat decerebrated at the upper border of the pons, Miller and Sherrington ¹⁰ were able to elicit well-coordinated swallowing movements not only by mechanical stimulation of the pharynx but by electrical stimulation of the inferior fovea of the medulla, overlying the dorsal nucleus of the vagus nerve. Discrete destruction of the substance of the medulla at this level had previously been shown to abolish deglutition.¹¹ Jaw movements resulting from buccal stimulation of animals in the experiments of Miller and Sherrington were restricted to opening of the mouth. Bazett and Penfield ¹² decerebrated cats by a section extending horizontally forward from the superior colliculus. These animals not only swallowed but exhibited chewing movements when the oropharynx was stimulated. Bremer ¹³ demonstrated a variety of oral responses in cats and rabbits, including rhythmic reflex mastication from stimulation of the buccal commissures, which persisted, though with diminished activity, when the plane of decerebration passed just anterior to the pons (see also Magnus ¹⁴).

Upon this bulbopontile mechanism, pathways converge from the corticobulbar system and via the hypothalamus from the older rhinencephalic structures.

With regard to the older system, Rioch and Brenner ¹⁶ demonstrated marked salivation, irregular chewing, chop licking, and swallowing on stimulation of the tuberculum olfactorium and pyriform lobe in decorticate cats and opossums. In a similar preparation, Schaltenbrand and Cobb ¹⁶ observed movements of the nose and whiskers, salivation, chewing, and licking movements from electrical stimulation of the exposed anterior commissure. The functional value of this system is attested by the studies of decorticate preparations.¹⁷ On the basis of similar studies, Bard

Peristalsis in Rabbits Under Normal and Some Experimental Conditions, Am. J. Physiol. 18:347-361, 1907. Cannon, W. B., and Lieb, C. W.: The Receptive Relaxation of the Stomach, ibid. 29:267-273, 1911. Carlson, A. J.: Contributions to the Physiology of the Stomach: III. The Contractions of the Empty Stomach Inhibited Reflexly from the Mouth, ibid. 31:212-222, 1913.

10. (a) Miller, F. R., and Sherrington, C. S.: Some Observations of the Bucco-Pharyngeal Stage of Reflex Deglutition in the Cat, Quart. J. Exper. Physiol. 9:147-186, 1915-1916. (b) Sherrington, C. S.: Reflexes Elicitable in the Cat from Pinna, Vibrissae and Jaws, J. Physiol. 51:404-431, 1917. (c) Miller, F. R.: The Cortical Paths for Mastication and Deglutition, ibid. 53:473-478, 1920.

- 11. Marckwald: Ztschr. f. Biol. 25:46, 1889; cited by Miller and Sherrington. 10a
- 12. Bazett, H. C., and Penfield, W. G.: A Study of the Sherrington Decerebrate Animal in the Chronic as Well as the Acute Condition, Brain 45:185-265, 1922.
- 13. Bremer, F.: Physiologie nerveuse de la mastication chez le chat et le lapin, Arch. internat. physiol. 21:308-352, 1923.
- Magnus, R.: Beiträge zum Problem der Körperstellung: I. Stell-Reflexe beim Zwischenhirn- und Mittelhirnkaninchen, Arch. ges. Physiol. 163:405-490, 1916.
- Rioch, D. M., and Brenner, C.: Experiments on the Corpus Striatum and Rhinencephalon,
 J. Comp. Neurol. 68:491-507, 1938.
- Schaltenbrand, G., and Cobb, S.: Clinical and Anatomical Studies on Two Cats Without Neocortex, Brain 53:449-488, 1931.
- 17. Goltz: Arch. ges. Physiol. **51**:570, 1892; cited by Bremer. Gad: Arch. f. Anat. u. Physiol., p. 540, 1891; cited by Bremer. Arch. f. Anat. u. Physiol., p. 209, 1900; cited by Bremer. Dusser de Barenne: Arch. néerl. physiol. **4**:31, 1920; cited by Bremer.

and Rioch ¹⁸ concluded that the retention of basal olfactory areas plus the hypothalamus, subthalamus, and reticular substance of the brain stem was sufficient for the elaboration of highly complicated feeding reactions.

The results of hypothalamic stimulation are not agreed upon. Motor effects on gastric activity have been reported from stimulation of the tuber cinereum by Beattie, ¹⁹ and again by Beattie and Sheehan. ²⁰ A similar effect was noted by Heslop ²¹ from the anterior region of the hypothalamus, whereas stimulation of the posterior part of the hypothalamus produced a reverse, but less pronounced, effect. The only gastrointestinal effect noted by Kabat and associates ²² and Ranson, Kabat, and Magoun ²³ was a general inhibition of activity induced by excitation of the lateral hypothalamic area.

Clear-cut evidence regarding salivatory and masticatory response from the thalamus and hypothalamus is again lacking (detailed review by Magnus ²⁴). Salivation has been noted from excitation of the thalamus by Magnus ²⁴ and as a part of seizures initiated by intralaminal thalamic stimulation. ²⁵ In man, Penfield's ²⁶ instance of salivation during autonomic seizures produced by a tumor of the third ventricle pressing on the anterior, mesial, and superior aspects of the thalamus is of interest. Kabat and associates ²² reported salivation as a late phenomenon in emotional mimetic responses elicited by hypothalamic stimulation in unanesthetized cats. In anesthetized animals, Ranson and Magoun ²⁷ had previously noted the absence of salivation during careful thalamic and hypothalamic stimulation. Mastication with other somatic movements was seen by Sachs ²⁸ on stimulation of the anterior part of the ventral thalamic nucleus in monkeys. Magnus ²⁴ also reported the observation of various oronasal responses and licking from excitation of the

^{18,} Bard, P., and Rioch, D. M.: A Study of Four Cats Deprived of Neocortex and Additional Portions of the Forebrain, Bull. Johns Hopkins Hosp. 60:73-125, 1937.

^{19.} Beattie, J.: The Relation of the Tuber Cinereum to Gastric and Cardiac Functions, Canad. M. A. J. 26:278, 1932.

^{20.} Beattie, J., and Sheehan, D.: The Effects of Hypothalamic Stimulation on Gastric Motility, J. Physiol. 81:218-227, 1934.

Heslop, T. S.: The Hypothalamus and Gastric Motility, Quart. J. Exper. Physiol. 28:335-339, 1938.

^{22.} Kabat, H.; Anson, B. J.; Magoun, H. W., and Ranson, S. W.: Stimulation of the Hypothalamus, with Special Reference to Its Effect on Gastro-Intestinal Motility, Am. J. Physiol. 112:214-226, 1935.

^{23.} Ranson, S. W.; Kabat, H., and Magoun, H. W.: Autonomic Responses to Electrical Stimulation of Hypothalamus, Preoptic Region and Septum, Arch. Neurol. & Psychiat. 33:467-477 (March) 1935.

^{24.} Magnus, W. O. C.: Über die Zentren für das Lecken und Kauen, Monatsschr. Psychiat. u. Neurol. 110:193, 1945.

Hunter, J., and Jasper, H. H.: Effects of Thalamic Stimulation in Unanesthetized Animals, Electroencephalog. & Clin. Neurophysiol. 1:305-324, 1949.

^{26.} Penfield, W.: Diencephalic Autonomic Epilepsy, A. Res. Nerv. & Ment. Dis., Proc. (1928) 9:645-663, 1930.

^{27.} Ranson, S. W., and Magoun, H. W.: Respiratory and Pupillary Reactions Induced by Electrical Stimulation of the Hypothalamus, Arch. Neurol. & Psychiat. 29:1179-1194 (June) 1933.

^{28.} Sachs, E.: On the Structure and Functional Relations of the Optic Thalamus, Brain 32:95-186, 1909.

6

ventral thalamic nucleus, the region overlapping in part the arcuate nucleus. In addition, the corpus callosum was noted to carry fibers initiating licking and chewing on stimulation.²⁹

Electrical stimulation of the inferior portion of the sensorimotor region of the cerebral cortex has produced mastication, deglutition, and salivation alone or in combination in a great variety of animals. Sachs, Brendler, and Fulton in noted that salivation was also produced by excitation of the orbital gyri in monkeys. Rhythmic oral responses to cortical stimulation, of either a sucking or a masticatory nature, are present in newborn animals. Rhythmic oral responses to cortical stimulation, of either a sucking or a masticatory nature, are present in newborn animals. Rhythmic oral responses to cortical stimulation, and Fisher so graph sological and anatomical means. Ranson, and Fisher confirmed this pathway in cats by stimulation with the Horsley-Clarke apparatus and ruled out the substantia nigra as an intercalary center for chewing, such as had been postulated by earlier workers. In their experiments, chewing, which was noted on stimulation

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30. (a) Beevor, C. E., and Horsley, V.: III. A Further Minute Analysis by Electric Stimulation of the So-Called Motor Region (Facial Area) of the Cortex Cerebri in the Monkey (Macacus Sinicus), Phil. Tr. Roy. Soc., S. B. 185:39-82, 1894. (b) Mann, G.: On the Homoplasty of the Brain of Rodents, Insectivores, and Carnivores, J. Anat. & Physiol. 30:1-35, 1895. (c) Simpson, S., and King, L.: Localization of the Motor Area in the Sheep, Quart. J. Exper. Physiol. 4:53-65, 1911. (d) Leyton, A. S. F., and Sherrington, C. S.: Observations on the Excitable Cortex of the Chimpanzee, Orang-Utan, and Gorilla, ibid. 11:135-222, 1917. (e) Lashley, K. S.: Studies of Cerebral Function in Learning: III. The Motor Areas, Brain 44:255-285, 1921. (f) Rogers, F. T.: An Experimental Study of the Cerebral Physiology of the Virginian Opossum, J. Comp. Neurol. 37:265-315, 1924. (g) Magoun, H. W.; Ranson, S. W., and Fisher, C.: Corticifugal Pathways for Mastication, Lapping and Other Motor Functions in the Cat, Arch. Neurol. & Psychiat. 30:292-308 (Aug.) 1933. (h) Smith, W. K.: Motor Cortex of the Bear (Ursus americanus), ibid. 30:14-39 (July) 1933. (i) Penfield, W., and Gage, L.: Cerebral Localization of Epileptic Manifestations, A. Res. Nerv. & Ment. Dis., Proc. (1932) 13:593-613, 1934. (j) Foerster, O.: The Motor Cortex in Man in the Light of Hughlings Jackson's Doctrines, Brain 59:135-159, 1936. (k) Penfield, W., and Boldrey, E.: Somatic Motor and Sensory Representation in the Cerebral Cortex of Man as Studied by Electrical Stimulation, ibid. 60:389-443, 1937. (1) Walker, A. E., and Green, H. D.: Electrical Excitability of the Motor Face Area: A Comparative Study in Primates, J. Neurophysiol. 1:152-165, 1938. (m) Crouch, R. L., and Thompson, J. K.: Autonomic Functions of the Cerebral Cortex, J. Nerv. & Ment. Dis. 89:328-334, 1939. (n) Rasmussen, T., and Penfield, W.: Further Studies on the Sensory and Motor Cerebral Cortex of Man, Federation Proc. 6:452-460, 1947. (o) Ferrier.4d (p) Sherrington.10b (q) Garol.4e (r) Penfield and Rasmussen.4g

31. Sachs, E.; Brendler, S. J., and Fulton, J. F.: The Orbital Gyri, Brain 72:227-240, 1949, 32. Henry, E. W.: Somatic Motor Responses Produced by Electrical Stimulation of the Cerebral Cortex of New-Born and Young Kittens, Federation Proc. 2:21, 1943. Hines, M.: The Motor Areas, ibid. 6:441-447, 1947.

33. Réthi: Sitzungsb. d. k. Akad. d. Wissensch. Math-naturw. Cl., Wien 102:359, 1893; cited by Magoun and others. Og Carpenter: Zentralbl. f. Physiol. 9:337, 1895; cited by Miller. Og Conomo, C. J.: Die centralen Bahnen des Kau- und Schluckactes, Arch. ges. Physiol. 91:629-643, 1902. Rioch, J. M.: The Neural Mechanism of Mastication, Am. J. Physiol. 108:168-176, 1934. Miller. Og Conomic Mathematical Mechanism of Mastication, Am. J. Physiol.

of the most anterior regions just below the cortex of the anterior composite gyrus (orbital gyrus), was replaced by lapping movements at the point of formation of the internal capsule and was not again noted at lower levels. The lowest response of rhythmic lapping movements was observed from the dorsolateral surface of the cortical fiber bundles at the caudal edge of the pons, 2 mm. rostral to the motor nucleus of the trigeminal nerve. Direct stimulation of this nucleus produced only steady closure of the jaw.

Intestinal motor effects have been obtained from the premotor area of both carnivores and primates.³⁴ On the other hand, Sheehan ³⁵ had previously reported only inhibition of gastric motility by stimulation of the premotor and frontal areas in macaques. Spiegel, Weston, and Oppenheimer ³⁶ found the influence of premotor stimulation on gastric activity to be highly variable in dogs, and in six animals they pointed out a region in the posterior part of the anterior supra-sylvian gyrus (areas 3 and 5 of Klempin ^{4b}) stimulation of which produced either augmentation or inhibition of gastrointestinal activity. Stimulation in the region of the respiratory inhibitory area on the orbital gyrus of the same species has been shown by others to cause diminution both of tonus and of peristaltic amplitude of the stomach.³⁷ Babkin and Speakman ^{37b} also found that the infragenual cingular region in dogs had an inhibitory action.

Taken together, the previous investigations have reported in detail those responses which we have chosen to call as a whole the "feeding pattern." The object of the present study, therefore, is to outline the temporal sequence of the responses in the "feeding pattern" and to investigate, by means of multiple simultaneous recordings of function, the characteristics of the total response. Emphasis has been placed on a study of the coordination of the whole sequence rather than on a detailed observation of one of its component parts.

METHODS

Thirty-five dogs, averaging 11 kg. in weight, were used for these experiments. All had been fasted for 18 hr. Three types of anesthesia were used: 1. Intravenous administration of 4 cc. per kilogram of body weight of a solution of 1 gm. of chloralose and 10 gm. of urethan in 60 cc. water. 2. Intravenous administration of 1.5 mg. of morphine hydrochloride per kilogram of body weight and the chloralose-urethan mixture in one-fourth of the preceding dose. With these methods a small amount of ether was often required for the operative procedures. 3. Intravenous administration of 1.5 mg. of morphine hydrochloride per kilogram and ether. It was attempted

^{34.} Watts, J. W., and Fulton, J. F.: Intussusception—The Relation of the Cerebral Cortex to Intestinal Motility in the Monkey, New England J. Med. **210**:883-896, 1934. Fulton, J. F.; Kennard, M. A., and Watts, J. W.: Autonomic Representation of the Cerebral Cortex, Am. J. Physiol. **109**:37, 1934. Watts, J. W.: The Influence of the Cerebral Cortex on Gastrointestinal Movements, J. A. M. A. **104**:355-357 (Feb. 2) 1935. Fulton, J. F.: Functional Localization in the Frontal Lobes and Cerebellum, London, Oxford University Press, 1949. Fulton reports work done in his laboratory by Davey in which gastric motor responses had been evoked by stimulation of the premotor area.

^{35.} Sheehan, D.: Effect of Cortical Stimulation on Gastric Movements in the Monkey, J. Physiol. 83:177-184, 1934.

^{36.} Spiegel, E. A.; Weston, K., and Oppenheimer, M. J.: Postmotor Foci Influencing the Gastrointestinal Tract and Their Descending Pathways, J. Neuropath. & Exper. Neurol. 2:45-53, 1943.

^{37. (}a) Bailey, P., and Sweet, W. H.: Effects on Respiration, Blood Pressure and Gastric Motility of Stimulation of Orbital Surface of Frontal Lobe, J. Neurophysiol. 3:276-281, 1940. (b) Babkin, B. P., and Speakman, T. J.: Cortical Inhibition of Gastric Motility, ibid. 13:55-63, 1950.

on all occasions to abolish spontaneous movements of the animal but to retain the lid reflex. Frequently bradycardia was evident in animals anesthetized with the morphine-chloralose-urethan mixture; this is to be noted in Figures 3 and 4.

All animals were equipped with a tracheal cannula as soon as the induction of anesthesia was complete. Two thin rubber balloons, 5 cm. long and 4 cm. wide when undistended, were placed 10 cm. apart on a double-lumen tube (Miller-Abbott). This tube was introduced through a small cut in the ventral aspect of the cervical portion of the esophagus and was fixed in place by a purse-string suture. These balloons were distended with air to a pressure of 1 to 3 mm. Hg, so that the pressure exerted on the walls of the esophagus would not stimulate its contractions. The position of the balloons was always checked at autopsy.

A balloon of similar size was placed in the antral portion of the stomach, either through an incision in the duodenum just below the pylorus or through an incision in the cephalic portion of the gastric corpus. In the latter case, the tip of the balloon was fixed in the antrum by a sature running through the stomach wall just proximal to the pyloric sphincter. In either case the wound in the viscus was closed about the tube by a purse-string suture. Air to a pressure of 5 to 10 mm. Hg was placed in the antral balloon. The pressure was adjusted with some care, as there usually seemed to be a degree of distention optimal for gastric peristalsis.

In the 15 experiments dealing with the effects of peripheral nerve stimulation, one of the superior laryngeal nerves was sectioned, and to its central end a ligature was attached. The same thing was done to the right or the left vagus nerve, both ends being taken on ligatures. The nerves were stimulated by a shielded bipolar electrode supplied by an apparatus made at this Institute by Dr. H. Jasper and Mr. L. Geddes. This stimulator delivered a square-wave pulse with independently variable voltage, frequency, and wave duration up to an 80%-duty cycle.

In the 20 experiments entailing stimulation of the cerebral cortex, the anterior portion of the brain was exposed after the removal of the left eye and temporal muscle. The exposed cortex was protected by liquid petrolatum U. S. P. or by frequent application of a modified Ringer solution (Elliott's solution A³⁸) at 38 C. A bipolar silver electrode with tips 1 to 2 mm. apart was used for all stimulations and was supplied by the apparatus described above. Stimuli lasted from 10 to 60 sec., and the shorter were never repeated oftener than once a minute. Usually, several minutes were allowed between stimuli for a regular peristaltic pattern to be established by the stomach. In these experiments, the jaw, opened about 45 degrees, was attached to another pneumograph and thus could record either closing or further opening. Salivation was noted by counting the drops as they fell from the opened mouth and so cannot be considered of more than qualitative significance.

During the experiments the position of all stimulations was transferred to a standard brain diagram, which on subsequent evaluation was broken down into a rough areal distribution (Fig. 7). In the selection of responses, all were included for evaluation except those showing continued mastication or a general seizure following stimulation. Repeated contractions of the esophagus alone were not considered evidence of cortical after-discharge, as in highly reactive preparations they could be induced by a momentary esophageal distention and were seen in spontaneous swallowing when the animal was under very light anesthesia.

Closing of the abdomen was routinely done after placing the abdominal balloon, since it promoted the return of gastric peristalsis. A regular peristalsis of the pyloric antrum was felt to be very important for the proper interpretation of results. The possibility of abdominal contractions influencing the tracings of the pyloric antrum without such an action being recognized is an objection to this method. However, this factor was felt to be satisfactorily controlled by elimination of all results with a marked respiratory disturbance and, in some experiments, either by direct observation of gastric motility or by simultaneous recording from the balloon in the antrum and one placed free in the peritoneal cavity below the rectus muscles or the diaphragm.

RESULTS

Owing to the differing nature of the experiments, the results have been divided into two sections. The first (A) contains observations on the effects of stimulation of afferent nerves from the pharynx, esophagus, and stomach, and the second (B), the results of cortical excitation.

^{38.} Elliott's solution A contains, in grams per liter, 8.6 NaCl, 0.3 KCl, 0.2 CaCl₂ · 2H₂O, 0.3 MgSO₄ · 7H₂O, 1.0 dextrose (Elliott, K. A. C., and Jasper, H. H.: J. Neurosurg. **6**:140-152, 1949).

A. STIMULATION OF AFFERENT NERVES OF PHARYNX, ESOPHAGUS, AND STOMACH

Spontaneous Swallowing.—This was observed repeatedly in six animals; five of these had subsequent esophageal contraction, and in two contraction of the antrum followed. These observations were thought important because they testified to the normal character of the whole phenomenon (Fig. 2).

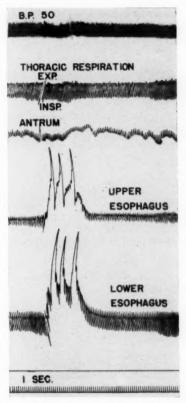


Fig. 2.—Spontaneous deglutition in a lightly anesthetized preparation. Note the deepened inspiration and slowed expiration immediately preceding the esophageal contractions.

Mechanical Stimulation of Pharynx.—In eight preparations the posterior wall of the pharynx was rubbed with a cotton swab. The most striking response, shown in Figure 3, included deglutition, contraction of the esophagus, relaxation of the cardia, and increased contractions of the pyloric antrum. In the animal concerned, antral contraction was repeatedly produced by pharyngeal stimulation insufficient to produce the rest of the complex. In general, however, the laryngeal movements of deglutition were the most constantly observed phenomena, with esophageal contractions next in frequency of occurrence.

Distention of Esophagus.—The arrangement for this experiment was the same as that described above, i. e., two balloons in the esophagus, or one balloon in the esophagus, the other in the cardiac sphincter and, of course, one balloon in the pyloric antrum. Sudden distention of one of these balloons in a reactive animal evoked rhythmic contraction of the esophagus over the distended balloon, which was quickly transmitted to the rest of the esophagus. (In the case of distention of the lower balloon this was in a caudorostral direction.) The esophageal contractions were followed by relaxation of the cardia and an increase in amplitude of the rhythmic

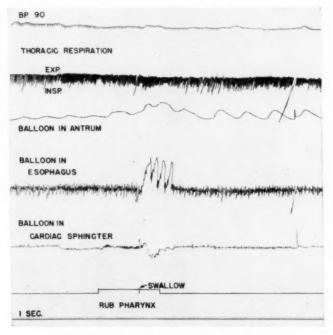


Fig. 3.--Effect of mechanical stimulation of the pharynx.

contractions of the pyloric antrum (Fig. 4), but, again, the frequency of occurrence of an antral response was less than that of the nondistended portion of the esophagus. Distention of the pyloric antrum was never followed by contractions of the esophagus. As before, occasional instances occurred in which the antrum contracted in response to distention of the esophagus without esophageal contractions. Section of one vagus nerve did not abolish the effect of distention, but section of both vagus nerves abolished this reflex altogether.

Stimulation of Superior Laryngeal Nerve.—Stimulation of the central end of the sectioned superior laryngeal nerve evoked repeated swallowing movements in all animals. This reflex proved to be one of the most constant and easily elicited. Respiration was altered, and effects ranging from expiratory apnea to marked rise

in frequency and amplitude, with struggling, were seen. The latter effect was seen more frequently with high current intensities; so the voltage was limited to that just producing swallowing in these experiments. The blood pressure response, when present, was characteristically a slight fall, associated with a slowing of the pulse.

In several experiments stimulation of the superior laryngeal nerve produced the whole motor complex described above and inhibition of the heart (Fig. 5). In other experiments only a few of these phenomena followed the deglutition, but the order in which they appeared was always rostrocaudal. On the other hand, movements

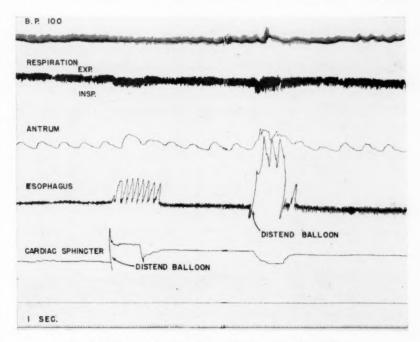


Fig. 4.-Effect of distention of the esophagus and cardiac sphincter.

of the esophagus, cardiac sphincter, and antrum were seen without detectable preceding oscillations of the larynx. 38a

Section of one vagosympathetic trunk in the neck, whether right or left, had no effect on the complex following deglutition induced by any method. In no instance following section of both vagus nerves in the neck were effects obtained from the esophagus, cardiac sphincter, or antrum.

³⁸a. In those experiments in which stimulation of the superior laryngeal nerve resulted in swallowing only, it was often possible to obtain additional contractions of the esophagus and stomach by administration of 1 to 2 mg. of physostigmine salicylate or 0.5 mg. of neostigmine bromide to an animal of 10 kg. Never, however, did this result in the onset of regular peristalsis in a previously inactive or hypoactive stomach. The contractions, though often powerful, made interpretation of results difficult, owing to their irregularity.

Effect of Stimulation of Superior Laryngeal Nerve on Heart Rate and on Antral Motility.—The close relationship of the various centers in the medulla oblongata is well shown in the following observation. In Figure 5 the central end of the superior laryngeal nerve was stimulated for 15 sec. This induced the whole complex response, namely, swallowing, inhibition of respiration, contractions of the upper esophagus, slowing of the heart rate, and increased antral contractions. Despite the fact that neostigmine or any similar drug was not used, there was a long after-effect of stimulation. For 2 min. and 40 sec. the heart rate was slowed, and during the same period the contraction of the pyloric antrum was increased.

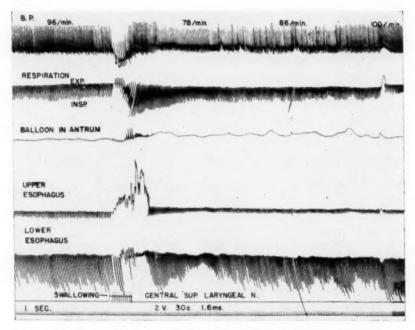


Fig. 5.-A long-lasting response to stimulation of the central end of the superior laryngeal nerve.

Stimulation of Central End of Vagosympathetic Trunk.—The effects on blood pressure consisted most commonly of bradycardia and a pressor response, while respiration responded as to central stimulation of the superior laryngeal nerve.

The most striking effect was that rhythmic esophageal contraction could definitely be separated from detectable laryngeal movements of swallowing. Section of the esophagus in the neck also had no effect on the thoracic contractions. Section of both vagus nerves abolished the peristalsis completely (Fig. 6). The responses of the antral portion of the stomach were contradictory. In six of 12 preparations in which this was recorded, the antrum showed various responses, which were again relatively constant for the given preparation but ranged from loss

of amplitude of the contractions, to decreased antral tonus followed by contraction, to increased amplitude of the antral contractions alone. Occasionally definite antral effects were again observed without other effects related to swallowing.

As the work progressed, it became increasingly apparent that under experimental conditions deglutition initiated by afferent stimulation had certain requirements and that its component parts might be obliterated by anesthesia. These requirements and variations in pattern may be roughly outlined as follows: 1. The response of the stomach usually required spontaneous peristalsis as a background. Contraction

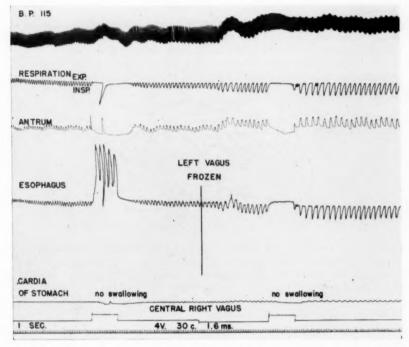


Fig. 6.—Effect of stimulation of the central end of the right vagus nerve. Note the dissociation of esophageal peristalsis and palpable movements of swallowing of the thyroid cartilage and the dependence of the former upon an intact vagus nerve.

of the stomach without some preexisting activity was rare. 2. An antral response, whether inhibitory or augmentatory, remained rather constant for a given preparation. 3. In general, those reflex responses which would be voluntary in the normal animal were the most resistant to anesthesia. An exception was the occasional finding that esophageal contractions might not be preceded by palpable laryngeal movements of deglutition (Fig. 6). 4. If, for some reason, one part of the tract did not respond, there still might be centrally coordinated activity of the other portions. Particularly striking, however, was the fact that this activity was always temporally oriented in a rostrocaudal direction.

Except for the somewhat variable gastric response, due presumably to the intrinsic nervous system of the stomach, the act of swallowing was characteristically inflexible in its sequence in that under adverse circumstances the responses, if present, performed without modification. It is a mass reflex involving not only the food passageway but the respiratory apparatus and, what is more difficult to fit into the teleologic pattern, the cardiovascular system. Deglutition, therefore, appears to be the product of a system in which many functions are interlocked in physiological equilibrium. Such a system anatomically would seem most probably located in the phylogenetically old reticular substance of the brain stem.

B. STIMULATION OF CEREBRAL CORTEX

On the basis of electrical stimulation, it was possible to divide the anterior portion of the cortex (Fig. 7) into an active strip running inferiorly on the anterior composite gyrus just lateral to the pre-Sylvian sulcus and the largely inactive parallel strips lateral to this and on the gyrus proreus. The responses of the more autonomous structures, especially the stomach, were found to be considerably more

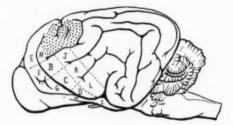


Fig. 7.-Arbitrary division of the anterior cerebral cortex of the dog.

variable than functions which would normally be under voluntary control. In each case the voltage threshold for an area in the sigmoid region producing limb movements was determined and then compared with that needed for response on the orbital surface. In rare instances the threshold was the same or lower, but in the great majority an increase of 25 to 100% in the voltage was required to elicit the effects noted below.

Region of Mesial Anterior Composite Gyrus and Pre-Sylvian Sulcus.—This region, composed of areas A, B, C, and D (Fig. 7) proved to be the most responsive, especially as the pre-Sylvian sulcus was approached. The width of this field, perpendicular to the pre-Sylvian sulcus, was greatest just below the coronal sulcus but diminished inferiorly.

In the superior portion of region A a mild pressor response and an augmentation of respiration were commonly elicited. The latter consisted largely of an increase in frequency, although the amplitude of respiration might be increased as well. In the inferior part of this region these effects dropped out. On stimulation high in area A the jaw registered an opening movement and the tongue was occasionally protruded, usually in the midline. Inferiorly, although rhythmic mastication was frequently obtained, it often had the curious character of further opening of the mouth with closure not beyond 45 degrees; thus, it was traced above the level of the base line

(Fig. 8). Salivation was never seen from the upper portion, but once from the inferior portion, of area A. Esophageal contraction was rare, and on two occasions a diminution of antral peristalsis occurred, again from the inferior portion of region A.

In area B the beginning of the "orbital-surface" phenomena was observed. The effects on the blood pressure level varied but were marked by the occasional appearance of coincident bradycardia. Respiration was inhibited, with primarily a diminution in frequency, although the response varied from loss of amplitude to expiratory apnea. Tongue movements were largely those synchronous with chewing; i. e., the

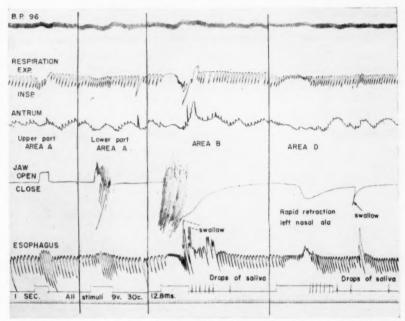


Fig. 8.—Responses of the jaw, salivation, and deglutition to stimulation (left to right) of the upper and lower portions of area A, area B, and area D, respectively (see Fig. 7).

tongue was held in the mouth and moved inward and outward as the jaws were closed and opened. Esophageal contractions were present in four animals, and salivation occurred in two.

Area C gave the most diverse and constant effects (Fig. 9). With few exceptions, there was inhibition of respiration, with the frequent appearance of periods of apnea in expiration. A pressor response was the most striking effect on blood pressure and was occasionally accompanied with bradycardia. Chewing was prominent, with tongue movements, as described for area B. Several preparations showed chewing that was not attended with opening of the mouth beyond the base line opening of 45 degrees. Salivation was nearly invariable and often profuse, but well related

to the periods of stimulation. Spontaneous salivation was never noted. There was frequent swallowing and esophageal contraction. Antral responses were seen oftenest from this area, i. e., in one-half the preparations. The response was a decrease in amplitude of the peristaltic waves. In the few cases in which contraction of the stomach appeared to be present we could not be certain that it was not due to respiratory changes or some other artefact.

In area D, blood pressure and respiratory responses were much as in area C except that expiratory apnea was infrequent. Only one-half the animals showed jaw movements, and the characteristic response was a sustained closure (Fig. 8).

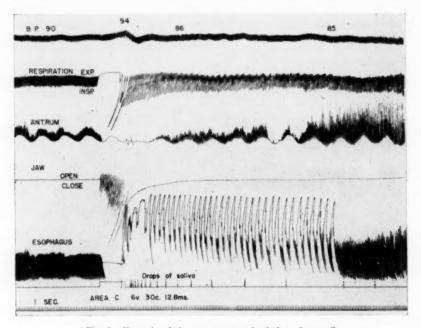


Fig. 9.—Example of the response to stimulation of area C.

When mastication occurred, there were rhythmic movements of the tongue in the midline. Throughout the series, deviation of the tongue was infrequent in comparison with midline movements.

Gyrus Proreus (Areas E, F, G, and H).—Stimuli producing marked effects lateral to the pre-Sylvian sulcus proved ineffective on the gyrus proreus even when carried to 1 mm, from the medial lip of the pre-Sylvian sulcus. Stimulation of the lateral portion of the olfactory tract and pyriform region (I) was noted to cause respiratory irregularities and twitching of the ipsilateral nasal ala. Salivation once followed stimulation of the lateral olfactory tract (area H), as did esophageal contraction in another animal. Area F in one preparation repeatedly produced esophageal contraction.

Lateral Anterior Composite Gyrus (Areas J, K, and L).—The lack of response in this region, in contrast to the more medial portions, was as striking as that of the gyrus proreus, although lacking the anatomical dividing line provided by the pre-Sylvian sulcus in the latter. As in the gyrus proreus, vasomotor responses were rare, and the infrequent respiratory effects were inhibitory in character. The responses from the medial anterior composite gyrus area spread farthest lateralward at the level of area B. Thus, the only feeding responses from the lateral anterior composite gyrus were seen in area J. One animal responded with mastication, while two others showed inconstant inhibition of antral motility. Salivation and esophageal contraction were never observed.

Sigmoid Gyrus (Stippled in Figure 7).—The medial portion of the somatic motor region was not adequately explored, but stimulation of the lateral portions, from which movements of the arm and leg were produced, never elicited responses from the jaw, esophagus, or antrum, and salivation was never noted. Blood pressure responses were about equally divided between pressor and depressor, while the effect on respiration was predominantly excitatory.

Comment.—During this part of the investigation the same general principles of action of the esophagus and stomach were observed. There was an increased regularity of response of the proximal over the distal portions of the tract, but, again, on rare occasions contractions of the esophagus appeared on cortical stimulation without detectable preceding larvngeal movements. The susceptibility of the esophageal and gastric responses to suppression by anesthesia and the invariable rostrocaudal temporal orientation of the surviving responses were evident. The overwhelmingly inhibitory effect of cortical stimulation on the spontaneous motility of the pyloric antrum was, however, in contrast with the augmenter effect usually seen on stimulation of the sensory nerves from the pharynx and esophagus. We have no good explanation for this. The cardiovascular and respiratory responses were again nearly invariable, though not completely consistent in their degree and direction of reaction. The effect on respiration of stimulation of a cortical area productive of chewing, salivation, and swallowing, etc., was interesting because the character of the response did not seem to fit a logical feeding pattern. Specifically, the respiratory arrest lacked a well-defined temporal relation to deglutition.

COMMENT

By simultaneously recording several different functions, we were able in this investigation, with a single experimental situation, to confirm most of the previous work done on various parts of the complicated process of deglutition. The existence was established of a complex reflex initiated by swallowing and followed by contraction of the esophagus, relaxation of the cardiac sphincter, and, predominantly, augmented motility of the pyloric antrum. The responses of the esophagus and stomach appear to be mediated by impulses of central origin carried solely by the vagosympathetic trunks in the dog. The final proof of this statement was obtained by section of these nerves when deglutition remained a purely pharyngeal phenomenon.

Under normal circumstances, it appears that during the act of swallowing a mechanism is set off in the "center of deglutition" in the medulla oblongata. In a logical sequence, respiration is momentarily arrested and impulses are sent in order to the pharynx, larynx, esophagus, and stomach.

The coordination of deglutition with respiration is, of course, mandatory under normal conditions. Indeed, such was apparent in instances of spontaneous deglutition in dogs under light anesthesia in the present experiments (Fig. 2). These relationships were carefully studied by Miller and Sherrington, 10n who found, in addition, that the cardiovascular system was involved. In their cats, decerebrated through the mesencephalon, a well-marked inhibition of respiration synchronous with deglutition was found, and when rapidly repeated swallowing was induced, a slight quickening, then slowing, of the pulse rate and a brief rise of blood pressure resulted.

However, the components of this sequence may be separated on the basis of their susceptibility to suppression by noxious processes. Denny-Brown and Russell ³⁹ observed that during recovery from a head blow a decerebrated cat first failed to respond by deglutition when liquid was placed in the back of the mouth. Then, with further recovery, the animal would swallow, but without accompanying arrest of respiration to this stimulus. Lastly, the cooperation of respiration and deglutition was recovered, and the act assumed its normal functional character. In this regard, Meltzer ⁶ noted the following sequence on the basis of the effect of decreasing anesthesia. Under deep narcosis, deglutition might be induced in animals but was never followed by esophageal peristalsis if a bolus were present in the esophagus. Finally, in the lightest stage, deglutition followed by esophageal peristalsis occurred even in the absence of a bolus. In our experiments the disintegration of the swallowing pattern was frequently seen when the anesthesia was not carefully adjusted.

Aside from adding components to the feeding pattern (tongue and jaw movements, salivation), stimulation of the cerebral cortex gave results sufficiently resembling the effects of excitation of the afferent nerves of the most rostral part of the gastrointestinal tract to lead one to inquire as to the precise role the cerebral cortex plays in this function. In a few cases the cortical masticatory area as outlined by electrical stimulation was removed and the white substance stimulated beneath it. As others had found before us, the complicated response appeared unmodified by this mutilation. Further, the study of decerebrate preparations proves that the rhythmicity and coordination of the masticatory act are represented in their entirety in the pons and medulla. It would seem, therefore, that fibers descending from the cerebral cortex in the internal capsule are still on the afferent side of the reflex arc. Thus, the difference between stimulation of a sensory nerve and stimulation of the cerebral "motor" cortex would consist solely in exciting a neuron on the afferent side of the thalamocortical sensory analyzers, in the former, and on the efferent side of the sensory analyzers, in the latter.

Whether this ultimate representation of movement and autonomic function in the short neuron arcs of the reticular substance can be applied to other somatic movements cannot, of course, be answered here. However, after transection of its neural axis at the base of the skull, the frog affords a striking example of the degree to which somatic movement may be organized in the isolated spinal cord of a lower animal. The conservatism of Nature in changing structures and mechanisms which are of functional value would lead one to suspect that a system as efficient as this

^{39.} Denny-Brown, D., and Russell, W. R.: Experimental Cerebral Concussion, Brain 64:93-164, 1941.

might persist to some degree despite the rigors of ascending phylogeny. If the conception be accepted that all function, somatic and autonomic, is fundamentally represented in the reticular substance of the brain stem and spinal cord, the role of the cortical "motor" neuron then consists simply of forming a line of communication between the effector system below and the final result of the cortical analysis of present and stored afferent impulses. These corticofugal volleys would thus serve to increase the efficiency of the system by better suiting the action of the organism to the stimulus and, thereby, to decrease the number of pointless responses which would result from the unguided discharge of the reticular substance.

SUMMARY

In 15 anesthetized dogs, afferent stimulation, whether by mechanical stimulation of the pharynx, distention of the esophagus, or electrical stimulation of the central ends of the superior laryngeal and vagus nerves, appeared to set off a mechanism in the central nervous system resulting in swallowing, contraction of the esophagus, relaxation of the cardia, and, predominantly, contraction of the pyloric antrum. Parts of this complex might be missing, but the remainder had a rostrocaudal temporal orientation. All effects except deglutition were lost after section of the vagus nerves in the neck.

In general, as the gastrointestinal tract was followed from the pharynx, which is normally under largely voluntary control, to the largely autonomous antral region of the stomach, the presence of responses to afferent stimulation became increasingly variable. The antrum was found to require a degree of background tonus and peristalsis to respond, and the response, whether augmentatory or inhibitory, would remain more or less constant as a characteristic of the given preparation.

Electrical stimulation of the anterior composite gyrus in 20 dogs showed that all the effects of the peripheral stimulation described above could be produced by cortical stimulation, except that the pyloric antrum responded primarily with inhibition, rather than with augmentation, of its activity. From the rostral portion of the anterior sigmoid gyrus augmenter effects on respiration, opening of the mouth and protrusion of the tongue were seen. Along the anterior composite gyrus, mastication, respiratory inhibition, salivation, swallowing, esophageal contraction, and, predominantly, inhibition of antral motility were the typical responses. The effects on blood pressure were variable, but occasional bradycardia occurred on stimulation of the masticatory area. The most active representation was found along the lateral lip of the pre-Sylvian sulcus.

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OCCLUSION OF THE MIDDLE CEREBRAL ARTERY

An Experimental Study

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AND
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CHICAGO

S IR ASTLEY COOPER ¹ in 1836 reported the results of a series of experiments in which he ligated the principal cervical arteries and nerves in various combinations and sequences. He concluded that death following pressure on the neck was due to cerebral anemia rather than to a direct nervous mechanism.

During the ensuing hundred years a large number of investigators studied the effects of generalized cerebral anemia of various degrees and of various durations.² The pathological picture of such cerebral anemia has been worked out in detail, and the susceptibility of various types of neurons of the brain, spinal cord and sympathetic nervous system to total and near total anemia has been well established.³

The study of focal cerebral anemia was initiated by Flourens'⁴ description, in 1847, of the effects of experimentally produced emboli in the cerebral vascular system. Subsequent studies of this type have elucidated further the dynamic mechanisms involved in small focal infarctions.⁵

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 Cooper, A.: Some Experiments and Observations on Tying the Carotid and Vertebral Arteries, Guy's Hosp. Rep. 1:458, 1836.

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 Flourens, J. P. M.: Note touchant l'action de diverses substances injectées dans les artéres, Compt. rend. Acad. sc. 24:905, 1847.

5. Villaret, M., and Cachera, R.: Les embolies cérébrales, Paris, Masson & Cie, 1939.

Larger focal areas of anemia have been studied experimentally by clipping the main intrinsic cerebral arteries intracranially. Petersen and Evans 6 clipped the middle cerebral artery in a series of monkeys and studied the histological changes in the resulting infarcts. Rasmussen 5 showed that clipping the middle cerebral artery in the dog likewise produced a gross infarct and pronounced hemiparesis, whereas clipping the anterior and posterior cerebral arteries did not produce significant brain damage. Watts 8 found in the monkey that clipping the anterior cerebral artery did not result in any appreciable neurological changes. Campbell and Forster of clipped the anterior cerebral artery in the monkey at various sites and estimated the typical distribution of this artery from studies of the resulting histological changes. Globus, Epstein, Green, and Marks 10 produced hemorrhagic infarcts in dogs by clipping the middle cerebral artery and subsequently producing an elevation in the systemic blood pressure. Thus it is established that, as is the case in man, occlusion of the middle cerebral artery in the monkey and dog produces an area of infarction in the brain and hemiparesis of significant proportion. There are, however, no data available on the effects of temporary occlusion of this artery in either of these experimental animals.

The objectives of this study were (1) to determine how long a temporary occlusion of the middle cerebral artery must be maintained in order to produce an infarct comparable to that produced by permanent occlusion of the artery, (2) to determine how long a temporary occlusion of the middle cerebral artery can be maintained without producing an infarct, and (3) to study the electroencephalographic changes associated with various periods of occlusion of the middle cerebral artery. These electroencephalographic changes will be the subject of a separate report.

PROCEDURE

The experimental animal was the monkey (Macaca mulatta). The right middle cerebral artery was permanently occluded in nine animals by transecting the artery between two clips placed as close to the point of origin from the circle of Willis as possible. These animals were killed at intervals of 30 min., 3 hr., and 2½, 5, 17, 22, 24, 30, and 56 days, respectively, after the occlusion, in order to study the variability in the infarcts produced and to determine the optimum time in which to study the results of temporary occlusion of the artery.

In 10 monkeys the artery was occluded for periods varying from 10 to 52 min. by means of a tiny spring clip applied as close as possible to the point of origin of the middle cerebral artery from the circle of Willis.

In a control experiment (Monkey 7) the artery was exposed and prepared for clipping in the usual manner and the retraction maintained for 10 min., but without any occlusion of the artery being carried out.

A condensed protocol describing a typical experiment follows.

Petersen, J. N., and Evans, J. P.: The Anatomical End Results of Cerebral Arterial Occlusion; Experimental and Clinical Correlation, Tr. Am. Neurol. A. 63:88, 1937.

^{7.} Rasmussen, T. B.: Experimental Ligation of the Cerebral Arteries of the Dog, Thesis, University of Minnesota, 1938.

^{8.} Watts, J. W.: Ligation of the Anterior Cerebral Artery in Monkeys, J. Nerv. & Ment. Dis. 79:153, 1934.

^{9.} Campbell, J. B., and Forster, F. M.: The Anterior Cerebral Artery in the Macaque Monkey, J. Nerv. & Ment. Dis. 99:229, 1944.

^{10.} Globus, J. H.; Epstein, J. A.; Green, M. A., and Marks, M.: Focal Cerebral Hemorrhage Experimentally Produced, J. Neuropath. & Exper. Neurol. 8:113, 1949.

MONKEY 2.—Nov. 2, 1948; male; weight 9¼ pounds (4.2 kg.); 30-min. occlusion.

Anesthesia was induced by intravenous injection of crystalline pentobarbital, 11 the dose being 1 grain per pound (0.13 gm. per kilogram) of body weight. Through the same needle 20 cc. of a 50% sucrose solution was injected to shrink the brain and facilitate exposure of the

Fig. 1.-Skin incision.



Fig. 2.—Operative exposure of the right cerebral hemisphere, with electrodes in place for electrographic recording and the temporal lobe retracted. The high lights at the tip of the retractor are on the middle cerebral artery.

artery. A control electroencephalographic record was made from each side of the head. A skin incision was made, as shown in Figure 1; the zygomatic process of the right temporal

^{11.} The crystalline pentobarbital sodium used in these experiments was supplied through the courtesy of the Abbott Laboratories, North Chicago, Ill.

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bone was removed, and the temporal muscle was reflected posteriorly. A free bone flap of maximum size was fashioned, and the exposure was extended inferiorly by removing most of the remaining squama temporalis.

The dura mater was opened widely. The electroencephalographic electrodes were arranged on the cortex in two longitudinal banks of four electrodes each, and recording was begun. The right temporal lobe was retracted so as to expose the middle cerebral artery and the adjacent portion of the circle of Willis (Fig. 2). The middle cerebral artery was freed from its bed for a distance of about 1 cm. from its origin. Coincident with manipulation of the vessel visible pulsations disappeared from all the exposed cortical vessels. After a half-hour pulsations had reappeared. The spring clip was then applied to the middle cerebral artery 1 mm. from its

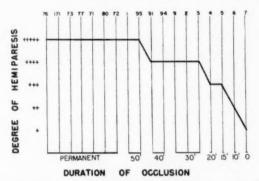


Fig. 3.—Relation of the degree of hemiparesis to the duration of occlusion of the middle cerebral artery. Data on Monkeys 75 and 70 are not included because of their short survival periods of 30 min. and 3 hr., respectively. The numbers of the remaining animals are given at the top of the graph.

In this chart +++++ indicates initial complete hemiplegia with marked weakness of the arm and moderate weakness of the leg still present at time the animal was killed; +++++, initial complete hemiplegia with moderate weakness of the arm and slight or no weakness of the leg at the time of killing the animal; +++, initial marked hemiparesis with only slight weakness of the arm remaining at the time of killing the animal; ++, definite awkwardness and infrequent use of the arm, lasting five days or less; +, minimal awkwardness in use of the arm, lasting two days or less.



Fig. 4 (Monkey 76; permanent occlusion).—Diagrammatic representation of area of infarction. Coarse stippling denotes gross infarction, and fine stippling indicates microscopic evidence of damage.

origin. Again, all visible cortical vessels ceased to pulsate grossly. The electroencephalographic recording was run continuously. At the end of 30 min, the clip was removed, and blood was observed to fill the adjacent distal portion of the artery. Electroencephalographic records were made at five-minute intervals. Twenty-two minutes later the cortical vessels were again pulsating normally. Thirty minutes after removal of the clip the electrodes were removed and the craniotomy wound was closed. At the conclusion of the procedure a second electroencephalogram was made from the scalp. Such recordings were made at subsequent intervals, and notes were taken daily about the degree of hemiparesis, hemianopsia, and hemianesthesia exhibited by the animal. On the 18th postoperative day the animal was killed by perfusion with sodium chloride solution and solution of formaldehyde U.S.P. through the carotid arteries.

Histological examination of the brain was carried out and the gross and microscopic extent of the infarction traced on diagrams of representative sections of the hemisphere.

RESULTS

A. Clinical Changes.—Permanent Occlusion: The behavior of these animals was essentially similar to that described in previous reports of permanent occlusion

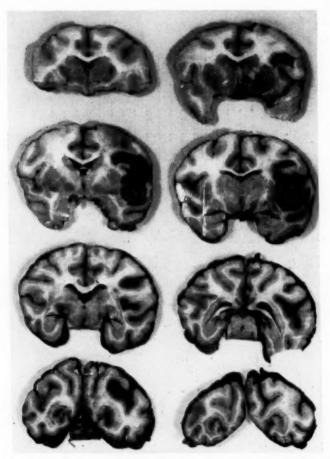


Fig. 5.—Coronal sections of brain of Monkey 1 (50-min. occlusion), showing hemorrhagic infarct,

of this artery in the dog ⁷ and monkey.⁶ The degree of motor impairment was remarkably uniform in spite of the variations in size of the infarcts produced. All the animals had complete left hemiplegia, which began to recede after the first few days, function returning more rapidly and more completely in the leg than in the arm. Hemihypalgesia was demonstrated in some of the animals early, but in others

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it could not be detected with certainty. Most animals clearly showed a homonymous hemianopsia during the first few days.

In only one animal (Monkey 72) of this group were any involuntary movements observed, and these consisted of irregular, ticlike twitchings of the left shoulder. Grossly, the infarct in this animal was neither more extensive than nor different in location from those of other animals in the series. No convulsive seizures were observed in any of the animals of this group.

Temporary Occlusion: In the animals subjected to temporary occlusion of the middle cerebral artery the degree of hemiparesis was directly proportional to the duration of the occlusion.

Figure 3 represents an attempt to depict graphically the relation of motor impairment to duration of occlusion. Occlusion of less than 15-min. duration produced transient hemiparesis only slightly greater than that seen in the control animal. At least 50 min. of occlusion was required to produce impairment as severe as that



Fig. 6 (Monkey 94; 40-min. occlusion).—Diagrammatic representation of areas of gross infarction (coarse stippling) and areas of microscopic ischemic changes (fine stippling).



Fig. 7 (Monkey 91; 40-min, occlusion).—Diagrammatic representation of area showing microscopic evidence of infarction.

following permanent occlusion. Convulsive seizures were observed in both animals subjected to 40-min. occlusion and in one of the animals with 30-min. occlusion.

B. Pathological Changes.—Permanent Occlusion: The pathological changes following permanent occlusion did not differ qualitatively in any important respect from those usually described in association with cerebrovascular occlusion of a major artery. The gross appearance depended on the time of survival; edema was at a maximum about the third day, and contraction of the infarct took place mainly during the second month of survival. Cyst formation was frequent. No hemorrhagic infarcts were found. After a survival period of 17 days the infarcted region was well demarcated and distortion due to edema or contraction was minimal.

The variation in the size of the infarcts was considerable. In most animals the infarct was fairly large (Monkey 76, Fig. 4), but one brain appeared almost normal grossly (Monkey 71), even though the animal had shown severe hemiparesis and autopsy showed that the middle cerebral artery had been transected.

The microscopic changes were similar to those described in detail by Gildea and Cobb. 3b

Temporary Occlusion: The infarcts, although on the whole they were proportional in extent to the duration of the occlusion, showed considerable variability. The 50-min. occlusion produced infarcts which were about as large as the average infarct following permanent occlusion (Fig. 5). Hemorrhagic infarction such as this occurred only after the two 50-min. occlusions. Infarction was less extensive in the animals with 40-min. occlusion (Fig. 6); in one of these no gross cortical infarct was seen (Fig. 7), although the animal sustained a rather severe degree of hemiparesis (Fig. 3). In only one of the three animals with 30-min. occlusions was there any gross cortical infarction, and this area of change was so situated that it may have been caused by the pressure of the occluding clip. Occlusions of less than 30-min. duration failed to produce gross cortical infarction. Figure 8 (Monkey 4) shows the absence of gross infarction following an occlusion of 20-min. duration. As shown in Figure 3, mild hemiparesis was present in this animal.

COMMENT

After 10 min. of occlusion recovery of motor function was complete; after 15 min. of occlusion slight residual impairment was still demonstrable at the time the animal was killed, 18 days after operation. It is interesting to compare these data



Fig. 8 (Monkey 4; 20-min. occlusion).—Diagrammatic representation of areas showing microscopic evidence of infarction.

with those given by Kabat and Dennis, ^{2e} who found that eight minutes of complete cerebral anemia of the entire brain caused permanent clinical impairment. The difference in these figures is readily explained on the basis of the important role of the collateral circulation when only one branch of the circle of Willis is occluded. The even lower critical figure (5 min. 45 sec.) suggested by Weinberger, Gibbon, and Gibbon ^{2f} may reflect the fact that in occluding the pulmonary artery they affected a still more complete degree of anemia of the entire brain.

To produce a degree of motor impairment similar in degree to that following permanent occlusion, it was necessary to occlude the vessel for 50 min.

Our knowledge of the distribution of the cerebral vessels is based mainly upon injection studies, the dissection of anatomical material, the clinical changes in human subjects with cerebrovascular lesions, and the correlation of these changes with the pathological findings. Since the final impression of the investigator depends upon the particular technique employed, no single representation of the details of the cerebral circulation should be considered complete and final.

Factors other than the technique of investigation complicate the picture. Cohnheim 12 stated that cerebral infarction could occur only in the absence of anastomoses

Cohnheim, J. F.: Untersuchungen über die embolischen Processe, Berlin, A. Hirschwald, 1872.

between the principal cerebral vessels, but subsequent studies by Fay,13 Cobb,14 and Pfeifer 15 furnish ample evidence that there are no end-arteries in the brain. This being the case, any boundary suggested between the territories of two main vessels must of necessity be an arbitrary one. The true physiological boundary undoubtedly varies not only from individual to individual but also from time to time in the same individual. If two or more lines of supply enter the same capillary network, the division of their respective territories must be a line across which no significant flow of blood is taking place; if the pressure in one of these lines of supply is lowered, the territory of supply of the remaining channels will shift in such a manner as to bring the complete system to a new state of hydrodynamic equilibrium. It is probable that such changes in the cerebral blood flow are in some degree occurring constantly. The region of infarction resulting from occlusion of the middle cerebral artery cannot, therefore, be said to represent the physiological distribution of the vessel; the latter is greater than the size of the infarct would indicate. The effect of the collateral circulation upon the size of the infarct is modified by the state of the contiguous capillary network at the time of occlusion. In these experiments the generalized vascular constriction already described presumably resulted in an extension of the region of infarction. The variation in the size of the infarcts produced may therefore in some measure be due not only to anatomical variations but also to transient physiological disturbances.

The size of the infarct resulting from permanent occlusions is modified by other variable conditions. If the experimental animal is killed early—"early" being arbitrarily defined as "within a week after operation"—the degeneration of the infarcted tissue is less obvious, and the region of infarction is likely to appear smaller than is actually the case. If, on the other hand, the animal is allowed to survive a month or more, the progressive shrinkage of the damaged tissue has the effect of making the infarct appear less extensive; furthermore, the distortion of the surrounding structures renders more difficult the task of accurately delineating the boundaries of the infarct. The results of these experiments appear to indicate that approximately three weeks is a satisfactory period of survival in studies of this nature.

The difficulty of achieving a constant degree of interruption of the vascular supply of the basal ganglia is reflected in the great variability of the lesions found in the deep structures. It is impossible to estimate accurately how much influence those deep lesions exerted on the behavior of the animals, but the transient nature of the disability in the control animal, Monkey 7, seems to indicate that damage to the basal ganglia produced by interrupting the perforating branches in preparing the artery for clipping was of minimal importance compared with the infarction produced by the occlusion of the middle cerebral trunk itself.

The fact that hemorrhagic infarcts occurred in only two of these animals, namely, Monkeys 1 and 95, in which the vessel had been occluded for 50 min., invites specu-

Fay, T.: Cerebral Vasculature: Preliminary Report of Study by Means of Roentgen Ray, J. A. M. A. 84:1727 (June 6) 1925.

^{14.} Cobb, S.: Cerebral Circulation: XIII. The Question of "End-Arteries" of the Brain and the Mechanism of Infarction, Arch. Neurol. & Psychiat. 25:273 (Feb.) 1931.

^{15.} Pfeifer, R. A.: Die Angioarchitektonik der Grosshirnrinde (Vorläufige Mitteilung), Monatsschr. Psychiat. u. Neurol. 65:166, 1927; Anastomosen der Hirngefässe, dargestellt am asphyktisch hyperämischen Kindergehirn, J. Psychol. u. Neurol. 42:1, 1931.

lation. Rouchoux,16 in 1884, suggested the concept of prehemorrhagic brain softening, and this idea was subsequently elaborated by others. Westphal and Baer 17 believed that intracerebral hemorrhage was preceded by angiospasm, which led to an anemic softening of the involved brain tissue, and that the subsequent return to a normal blood flow to the vessel was followed by a rupture of the vascular walls because of defective support by the adjacent brain tissue. Schwartz 18 proposed a somewhat similar hypothesis but stated the belief that an injurious stimulus in the region of a large vessel resulted in generalized spasm and stasis throughout its distribution, with extravasation, multiple nutritional defects, and, finally, petechial hemorrhages, fusion of which produced the picture of massive intracerebral hemorrhage, giving as his opinoin that in every instance it was preceded by a cerebral softening. Globus, Epstein, Green, and Marks,10 after occluding the middle cerebral artery in dogs and thereby producing a region of cerebral softening, raised the blood pressure by the injection of phenylephrine and were able thus to produce typical hemorrhagic infarcts. In the present series of experiments the sequence of events leading to the production of massive intracerebral hemorrhage may have been as follows: An occlusion of 50-min, duration resulted in damage to the walls of the vessel and to the temporarily anemic brain tissue. The blood pressure in the vessel was then allowed to return to the original level by removal of the clip. When the process of cerebral softening combined with degeneration of the vessel walls was sufficiently extensive, rupture of the vessel occurred in one or more places, with the result that massive cerebral hemorrhage was produced.

Reference should be made to a phenomenon which may to some extent have modified the results of these experiments, namely, the occurrence of vascular spasm. It was observed that any manipulation of the middle cerebral artery caused generalized contraction of the vessel walls. This was sufficiently marked to make it imperative to isolate the central portion of the artery quickly and positively, since after constriction had occurred the vessel was much more difficult to find. This constriction was not confined to the vessel which was being manipulated, for pulsations usually became imperceptible in all the vessels over the exposed hemisphere. In this connection, the observations of Villaret and Cachera ⁵ and Echlin ¹⁹ are relevant. It is probable that the sudden onset of local occlusion in a cerebral vessel not only deprives the brain of its blood supply in the distribution of that vessel, but also renders the whole cerebral hemisphere relatively anemic and therefore more vulnerable to the effects of the local process.

SUMMARY

The right middle cerebral artery was occluded in nine monkeys permanently and in 10 monkeys temporarily for periods varying from 10 to 50 min. During each experiment a continuous cortical electrogram was obtained, and electro-

Rouchoux, J. A.: Du ramollissement du cerveau et de sa curabilité, Arch. gén. méd.
 6:265, 1844.

^{17.} Westphal, K., and Baer, R.: Über die Entstehung des Schlaganfalles, Deutsches Arch. klin. Med. 151:1, 1926.

^{18.} Schwartz, P. H.: Die Arten der Schlaganfälle des Gehirns und ihre Entstehung, Berlin, Julius Springer, 1930.

Echlin, F. A.: Vasospasm and Focal Cerebral Ischemia, Arch. Neurol. & Psychiat.
 47:77 (Jan.) 1942.

encephalograms were made at intervals after operation. The postoperative survival period varied from three hours to 56 days after permanent occlusion and from 16 to 18 days after temporary occlusion. After 16 to 18 days the infarct was well demarcated and the distortion of anatomical structures was minimal.

Manipulation of the middle cerebral artery usually resulted in a marked constriction of all the vessels of the exposed hemisphere. Constriction always occurred at the site of manipulation, i. e., near the circle of Willis, and was observed also in the internal carotid artery. In most instances the caliber of the cerebral vessels returned to normal immediately or within a few seconds after the cessation of occlusion.

The degree of hemiparesis varied with the duration of occlusion. Occlusions of less than 15-min, duration produced only temporary impairment of motor function. To produce a degree of impairment as severe as that associated with permanent occlusion, it was necessary to occlude the vessel at least 50 min.

Clinical seizures were observed in three animals, following occlusions of 40, 40, and 30 min., respectively. Of the animals in which the vessel was permanently occluded, one had typical electroencephalographic seizures without observed clinical manifestations; another exhibited irregular twitching of the left shoulder.

With a few exceptions, the extent of gross infarction varied directly with the duration of occlusion. Occlusion of 50-min. duration produced an infarct about as large as that following permanent occlusion; the infarcts following shorter periods of occlusion were smaller. No gross cortical changes were observed after occlusions of less than 30-min. duration.

Hemorrhagic infarction occurred in two animals; in both these animals, the vessel had been occluded for 50 min. The relation of such experimental infarction to the concept of prehemorrhagic softening is discussed.

These findings represent the first available data on the changes associated with controlled temporary occlusion of a single important cerebral artery. It is hoped that this study will provide a technique and a basis for a critical experimental evaluation of therapeutic procedures employed in cerebrovascular thrombosis, embolism and hemorrhage.

IS THERE A SPECIFIC PERSONALITY IN TUBERCULOUS PATIENTS?

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THE IMPORTANCE of the neuropsychiatric problems of patients with pulmonary tuberculosis has long been recognized. This paper is based on three-years' experience with psychiatric problems at the Montefiore Hospital Country Sanatorium, Bedford Hills, N. Y., a 230-bed institution for patients with uncomplicated pulmonary tuberculosis. In addition to diagnosis and therapy, attention was focused on the question of whether there is a specific type of personality among persons who have pulmonary tuberculosis. This paper deals with the results of that investigation.

REVIEW OF LITERATURE

Munro,² Jelliffe and Evans,³ Dunbar,⁴ and others have stated that there is a characteristic personality pattern among persons with tuberculosis. This consists of selfishness, egotism, irritability, hypersensitivity, disregard for others, dependent cravings, passivity, and regressive tendencies. Mühl ⁵ listed 23 characteristics; Eyre,⁶ 10, and de Freitas,⁷ 4. On the other hand, Schultz,⁸ Brown,⁹ Forster and Shepard,¹⁰ Daniels and Davidoff,¹¹ and others expressed the opinion that the tuber-

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Hartz, J.: Tuberculosis and Personality Conflicts, Psychosom. Med. 6:17, 1944. Berle,
 B.: Emotional Factors and Tuberculosis, ibid. 10:366, 1948.

 Munro, D. G. M.: The Psychopathology of Tuberculosis, London, Oxford University Press, 1926.

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 de Freitas, C.: Introduction to Psychological Study of Pulmonary Tuberculosis, Neurobiologia 9:296, 1946.

Schultz, I. T.: Emotions of the Tubercular: A Review and an Analysis, J. Abnorm.
 Social Psychol. 37:260, 1942.

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10 Forster, A. M., and Shepard, C. E.: Abnormal Mental States in Tuberculosis, Am. Rev. Tuberc. 25:324, 1932.

11. Daniels, G. E., and Davidoff, E.: The Mental Aspects of Tuberculosis, Am. Rev. Tuberc. 62:5, 1950.

culous infection is superimposed on a preexisting personality, which may be of various types. We find ourselves aligned with the latter group.

There is general agreement, however, that tuberculosis accentuates the dependent, passive, and egocentric traits present in everyone. This is due not to the Koch bacillus itself, or to a toxin, but to the enforced lengthy bed rest which is the cornerstone of therapy. Fears of distortion of the body, of physical and socioeconomic limitation, and of death are certainly present in many patients. Hostility, resentment, resignation, depression, guilt, and anxiety are also encountered, but we find no convincing evidence that they are commoner in tuberculous patients than in those with other illnesses requiring long hospitalization or convalescence. There are some patients who, as Day 12 said, find their tuberculosis a "flight from frustration," but we feel they are relatively few. We share Wittkower's 13 view that "in the end the psychological mechanisms fail to explain why the patient falls ill with pulmonary tuberculosis."

The psychiatric problems encountered in tuberculosis have been well discussed by Merrill ¹⁴; Coleman, Furst and Hornbein ¹⁵; Hartz, ¹⁶ and Bellak. ¹⁷ Reaction to the diagnosis, whether of acceptance or rejection, is the first hurdle. Separation from loved ones is often the second problem. Concern over death, contagion, disfigurement, and social ostracism is probably universal among tuberculous patients. Worry over surgical procedures, economic readjustment, and possible breakdown is equally prevalent. The increasing awareness of the importance of these emotional factors in the care of the tuberculous patient is attested to by the greater role now played by psychotherapy in modern tuberculosis sanatoriums.

METHODS AND MATERIAL

Psychiatric services were rendered by a consultant psychiatrist, who spent one day a week at the sanatorium, and one full-time rehabilitation director, who was a clinical psychologist, and two psychiatrically trained social workers, each of whom spent two or three days a week at the institution. Referrals to the psychiatrist were made chiefly by the social workers and the rehabilitation director, and occasionally directly by the resident physicians. The number of psychiatric interviews with each patient varied widely, from two or three to 70 or 80, depending on the patient's need and on his ability to accept therapy. The psychiatrist gave a short orientation talk to all new patients each fortnight. This provided him an opportunity to see each patient very briefly, and to be seen by the patients, thus decreasing anxiety on the part of those who would be referred for diagnosis and therapy.

We did not study all patients, for comparison of the tuberculous patients with psychiatric symptoms and those who had no such apparent difficulties, but limited ourselves to persons referred because of emotional tensions. Of 118 patients who were seen, 9 had psychoses; 13 had organic neurological disorders; 6 had miscellaneous disturbances, and 90 had psychoneuroses. Our attention was focused on the last category, and here we found that the psychodynamics varied greatly. While each patient presented many traits, we found no one common factor, or group of factors, which characterized persons with pulmonary tuberculosis. We compared

^{12.} Day, G.: Observations on the Psychology of the Tuberculous, Lancet 2:703, 1946.

^{13.} Wittkower, E.: A Psychiatrist Looks at Tuberculosis, London, National Association for the Prevention of Tuberculosis, 1949, p. 137.

Merrill, B. R.: The Psychology of Tuberculosis Rehabilitation, Rehabilitation Service Series Bulletin No. 16, Office of Vocational Rehabilitation, Federal Security Agency, 1946.

^{15.} Coleman, J. V.; Furst, A., and Hornbein, R.: Psychiatric Contributions to the Care of Tuberculous Patients, J. A. M. A. 135:699 (Nov. 15) 1947.

^{16.} Hartz, J.: Human Relationships in Tuberculosis, Pub. Health Rep. 65:1292, 1950.

¹⁷ Bellak, L.: Psychiatric Aspects of Tuberculosis, Social Casework, 1950,

this group with patients seen in private or clinic psychiatric practice, where there was no symptom or sign of pulmonary tuberculosis. Illustrative case histories from each group are given, cases 1 to 5 being those of tuberculous patients and cases 1 A to 5 A, those of non-tuberculous psychiatric patients, seen on an outpatient basis, with a diagnosis of psychoneurosis, anxiety state.

CASE 1.-A German woman aged 31, single, contracted tuberculosis three months after arriving in the United States, in 1947. At the sanatorium she complained of severe depression, generalized fears, and occasional thoughts of suicide. Her childhood was characterized by ambivalence toward the parents, jealousy of a pretty younger sister, strong feelings of inferiority and masochism, strong perfectionistic and compulsive drives, and psychosexual maladjustment. Because of many depressive episodes, she was under psychiatric treatment for a year at the age of 16, with little benefit. During the war she lived in England, tried to seek approval by long hours of faithful work in a social agency, but never made close friends or felt emotionally at ease. At the sanatorium she was chronically tense, depressed, self-effacing, dependent, and submissive. Repressed hostility was strong, and she dared not express her emotions for fear of being rejected. All her occupational therapy activities, her letter writing, and translations from the German were meticulously done, and she checked and rechecked them constantly because of her compulsive need to be perfect. Suicidal thoughts became so strong at one point that she was given four electroshock treatments. These neither relieved her depression nor caused any ill effects in her pulmonary condition. The pulmonary diagnosis was tuberculosis of both upper lobes, far advanced, arrested. There was clinical and roentgenological improvement from the time of admission in April, 1947, until September of that year, with stabilization thereafter. Her tuberculosis has remained arrested for three years.

Comment.—The masochistic, compulsive traits and feelings of inferiority and depression were so chronic and severe that continued explanatory and supportive psychotherapy was imperative throughout her stay in the sanatorium. Active planning for her career was incorporated in the program, and she has been gainfully employed in a semiprotected environment for three years. Although she has not resolved her basic conflicts, which would require years of deep therapy, she has been aided in maintaining emotional equilibrium on a satisfactory social level.

CASE 1 A .- A single woman aged 32 was referred because of concern about overweight and feelings of depression. As a child she was ridiculed by her mother, who called her a "fat cow." She was completely rejected by both parents and was made to do housework until 1 and 2 a.m. after a full day at school. She was frequently beaten by her mother and was so fearful of the latter that she never told her mother anything. At the age of 9 yr. she was kidnaped; at the age of 12 she was raped; at the age of 14 she was badly frightened by a "practical joker," who made strange sounds outside her window. The mother suffered from asthmatic attacks, which she used effectively to keep the patient home. Both mother and daughter were compulsive in their neatness and rigid standards. The patient assumed all the responsibility for caring for her sick mother and invalid sister. Since the mother's death, the patient has felt bound by a promise always to look out for the family and has been the financial and emotional support of her four siblings. She has always been withdrawn, shy, passive, and compulsive in her desire to help others, masochistic in her complete refusal to accept praise or friendship, depressed, and given to talking of suicide. There were no symptoms or signs of a pulmonary lesion; the roentgenogram of the chest was normal, and her physical health has been good.

Comment.—Complete rejection as a child, the physical and sexual assaults, the compulsive neatness, the exaggerated sense of responsibility, and the masochistic traits were so chronic that the patient was frequently very depressed. Repression was so strong that ventilation required a great effort, but did relieve her chronic tension. She is still under treatment.

Case 2.—A married woman aged 31 first contracted tuberculosis at the age of 13, was treated for two years, and had reactivations at the ages of 20, 26, and 30. She was referred to the psychiatrist because of nervousness and restlessness. Her childhood had been very unhappy: Her father deserted; her mother had a severe compulsive neurosis, and her stepfather was apparently psychotic, though not hospitalized. The patient had six years of

schooling and a business course and then worked as a stenographer until her marriage, at the age of 27, to an alcoholic widower 15 yr. her senior. There were constant quarrels, physical beatings, and financial hardships. The patient was promiscuous all her life, with mild feelings of guilt. Her 3-yr.-old daughter admittedly interfered with the patient's having a good time. Usual precautions regarding rest for a person who has had tuberculosis were flagrantly ignored; she stayed out late at night as often as possible to escape domestic responsibilities. Each breakdown followed a period of much social life, emotional stress, and little rest. The sanatorium was a haven of refuge to her and she was unwilling or unable to face realities of the future. Her immaturity was pronounced, and she avoided all decisions whenever possible. She was narcissistic, dependent, friendly, and passive. Sexual desires were strong and freely exercised, with little sense of guilt. Her pulmonary diagnosis was chronic pulmonary tuberculosis, far advanced, with bilateral cavitations. With bed rest, pneumothorax (left), and partial pneumonolysis, she improved and was discharged with the disease arrested two and a half years after admission.

Comment.—Her inability to face reality and to make decisions, her dependence and passivity, together with the hostility toward her husband and her strong sexual desires, made the prognosis guarded from the outset. She enjoyed the opportunity of ventilating but wanted to become too dependent on the therapist. Her emotional immaturity and her mode of life probably contributed to her being run down physically and to the reactivation of her tuberculosis. Hospitalization relieved her temporarily of the necessity of making decisions. Psychotherapy gave her a small amount of understanding, and she was able to do satisfactory work of a clerical nature in a semiprotected environment.

Case 2 A.—A housewife aged 35 had complained of generalized tension since the birth of her third child, several months previously. Her parents were divorced when she was 7 yr. old. Her mother favored the other children, and the patient felt rejected. She fractured her leg in an automobile accident at the age of 8 yr., and the residual moderate disfigurement made her self-conscious. She was bright in school, shy, aloof, and unhappy under strong maternal domination. At the age of 23 she married a man who was "a gentleman," but with whom she was not in love. He had an epileptic attack shortly after marriage, and the patient felt he had deceived her because he had not told her of the seizures, from which he had been free for many years. The patient felt she was a martyr, actively sought sympathy, alienated friends by her excessive complaints, had an unsatisfactory sex life, and was still under the domination of her mother and one sister. The patient's oldest child, aged 7 yr., had a tic and enuresis. The patient was overtalkative, evasive, immature, passive, dependent, sought pity, and whined a great deal. Her physical health, except for the leg injury and chronic hay fever, was good. There were never symptoms or signs of pulmonary lesions. After three or four visits, she refused further psychotherapeutic help.

Comment.—The patient was immature, dependent, unable to face her mother's domination or her husband's illness, constantly sought attention and pity, and had no ego strength to look at her problems objectively or to accept psychiatric help. When seen a year later, she was unchanged emotionally. Her symptoms were serving the useful purpose of preventing her from making painful decisions and accepting realities.

Case 3.—A Hungarian, aged 23, had been hospitalized with tuberculosis for five years. His mother and three siblings were later found to have tuberculosis too. He was referred for psychiatric help because of tension, restlessness, and absorption in pessimistic philosophical literature. His childhood had been extremely traumatic, due to anti-Semitism and frequent stonings at school in Hungary, and very strict orthodoxy at home. Hostility to the mother was expressed in terms of chronic stomach ailments. He felt dependent on, but rejected by, the mother. Intellectual development was unusually good, but he never learned to socialize or to develop emotional security. Sexual matters were considered evil. Feelings of inferiority, dependence, repression of hostility, and escape into intellectual pursuits from the dangers of social intercourse were outstanding traits. His pulmonary condition was chronic tuberculosis, far advanced, bilateral, arrested; status post-thoracoplasty (right) and pneumothorax (left); laryngeal and endotracheal tuberculosis. His pulmonary condition improved after two months of streptomycin therapy in 1947.

Comment.—The patient was seen weekly for one and a half years with much improvement in self-assertion, psychosexual maturity, sociability, and adjustment to practical realities in the United States. While streptomycin greatly helped his pulmonary condition, and thus also his psychic state, psychotherapy was of great importance in making him more stable. For the past two years he has been studying accounting, has become more realistic, gained much self-confidence, and has greatly improved in socializing with both family and friends.

CASE 3 A .- A man aged 33 sought psychiatric help because of uncontrolled rage, sexual problems, and an unhappy marriage. He was the only child of a strict, idealistic, compulsive mother, who set very high standards for her son. Fear of failure to please his mother obsessed the boy; and, though he succeeded well in a material sense, he was emotionally restless and tense. He had high ideals, much egotism and stubbornness, and rarely admitted he was wrong. Though outwardly self-confident, he had strong feelings of inferiority and insecurity. Sexual difficulties with his wife led to a divorce and a second marriage, which was very compatible. As a boy he was exposed to considerable anti-Semitism but learned to defend himself with his fists. His interests were chiefly intellectual, and his intelligence was well above average. With psychiatric help he was able to recognize his unconscious hatred of his mother, and also of his father, and learned to overcome his fear of failure. His desire for approval from others and drive for power remained strong, but they no longer produced uncontrolled rage when he felt frustrated. His physical health was always good, and there was no subjective or objective evidence of pulmonary disease. The roentgenogram of the chest was normal.

Comment.—Fear of failure to meet the excessive demands of a compulsive mother led to unconscious hatred and resulted in his being outwardly egotistical, but inwardly insecure. He sought escape in intellectual achievements, which were considerable, but had to learn to face emotional needs in order to function effectively in a social milieu. He has adjusted well, and is a much more stable and happy person.

Case 4.—A married woman aged 37 first had pulmonary tuberculosis in 1935, a year after divorcing her first husband, and had reactivations in 1941, 1943, and 1946. She was referred to the psychiatrist because of feelings of tension and insecurity for many years. During her girlhood there were complete lack of affection and severe financial troubles. She married early to escape the poor home environment and suffered many physical, sexual, and emotional traumas from her husband, such as defending her sister against rape by her husband. She rebelled against domination by her mother, who was strict and cold; by her first husband, who was selfish and cruel, and by her second husband, who lost his love for her because of her illnesses. She was a shy child, jealous of a younger sister, sensitive, introspective, with much ambition, especially to write, and many mood swings. Hostility was repressed because of fear of repercussions. She received affection from no one except her three sons by her first husband, and she greatly overprotected the boys. There was a constant feeling of loneliness and frustration. Although she did not express the thought openly, sickness was a temporary release from overwhelming responsibilities and problems. Her pulmonary diagnosis was tuberculosis, far advanced, bilateral, arrested.

Comment.—Lack of emotional and financial security, repeated domination, and frustration because she could not assert herself caused chronic tension. This was greatly relieved by ventilation, a firm but sympathetic approach, and practical help from social agencies. After discharge from the sanatorium, she faced realities, secured a second divorce and has been supporting herself and her sons with successful determination.

Case 4.A.—A married woman aged 27 was referred because of severe depression and several suicidal attempts. She had been under psychiatric care, including three short periods of hospitalization for severe agitation, during the preceding year. Her father was alcoholic and had assaulted her several times before the age of 15. Both parents had rejected her, and she became shy and withdrawn, later rebelling against their wishes by many drinking and sexual escapades. She married at 21, had two children, but was deserted by her husband when she became emotionally sick. She became addicted to barbiturates for short periods and also suffered from bromide intoxication. She was extremely tense, depressed, narcissistic, unable to make decisions, and resentful against her parents, with whom she was forced by

financial circumstances to make her home. She was dependent, sexually maladjusted, and confused as to her aims and goals. Except for asthma as a girl, her physical health had been good. The roentgenogram of the chest was normal.

Comment.—Although her illness had many aspects suggesting psychosis, the diagnosis at two hospitals where she was treated and our impression was that of a severe pan-neurosis. There were chronic, marked rejection, domination, sexual conflict, escape into drug addiction, and suicidal attempts. No symptoms or signs of pulmonary tuberculosis were found.

CASE 5.—An American-born boy of Czechoslovakian parentage, aged 18, was discovered to have pulmonary tuberculosis in March, 1949, and was admitted to the sanatorium three months later. He was referred to the psychiatrist because of fear of meeting new people. The history revealed slow development in infancy, with many involuntary jerky movements, temper tantrums, and crying. The father was extremely strict, frequently beating his son. The mother tried to be more affectionate but was unable to withstand the pressure exerted on her by her husband. The patient, and later his younger brother, were placed in an orphanage at the age of 13. He mingled very little with the other children, never had a date with a girl, suffered guilt feelings over masturbation, and immersed himself in books. His intellectual ability was very good, his intelligence quotient rising from 80, on admission, to 140, four years later. Repeated neurological examinations, including electroencephalographic studies, showed a normal status. During psychotherapeutic sessions he trembled severely. There were strong feelings of inferiority, repressed hostility toward the father, inability to socialize, and psychosexual maladjustments. Lack of affection was pronounced: "I can't imagine myself being liked." His pulmonary diagnosis was tuberculosis of both upper lobes, moderately advanced, active, with improvement. He is still in the sanatorium.

Comment.—Some of this boy's problems were those of adolescence; some were neurotic fears and anxieties. He had been rejected throughout his life and never before had allowed an older person to take a prolonged personal interest in him. During the six months that he was under weekly psychiatric care he matured greatly, developed more self-confidence, and gained insight into sexual and social problems which had long plagued him. He needs further care, but at this writing his emotional growth has been very encouraging.

Case 5.A.—A girl aged 17 was referred because of nervousness, stuttering, and night-mares. She was the second of four children and was obese, shy, intelligent, passive, and submissive. Her father's death three years earlier had been a severe shock, and since then the mother had been very domineering. The mother insisted that the patient stay home from school to care for her 1 yr. old sister, while she (the mother) apparently did very little. The patient was tense, constantly wrung her hands, showed signs of compulsive neatness, and was fearful of opposing the mother. The latter was clever and used many subterfuges to keep the patient under control. With the aid of occasional visits to the psychiatrist and constant support from a psychiatric social worker, the patient's passivity, lack of self-confidence, and tension were decreased. She became more sociable with both boys and girls, acquired poise, and showed more interest in her appearance. She learned to express her hostility, though in guarded fashion, and succeeded in establishing emotional and financial independence of her possessive, yet rejecting, mother. Her physical history was not remarkable except for an intestinal resection (volvulus?) at the age of 9 yr., a mastoidectomy, and obesity. There was no evidence of pulmonary tuberculosis.

Comment.—Domination by a rejecting mother for selfish purposes was successfully overcome. The patient's passivity, dependence, tension, depression, and hostility were relieved by the sympathetic approach and reassurance from the social worker and the psychiatrist. She was able to attend college, made average grades her first year, made a good social adjustment, and maintained her independence. However, during her sophomore year she again became tense and had to leave school. Details of this episode are not available.

COMMENT

Although, of course, no two cases are exactly similar, it is felt that the mechanisms in the above paired cases are not without significance. Cases 1 and 1 A

illustrate the obsessive-compulsive and strong masochistic traits which resulted in depressed, withdrawn, shy, passive behavior. Yet these patients had much inner drive to assert themselves, and to the casual onlooker they were getting along satisfactorily in life. Both were so repressed that therapy was slow and painful, yet much desired. Dunbar's phrase, "half in love with death," would seem to apply equally to these patients. Cases 2 and 2 A are instances of immature, dependent, passive persons who refused to face reality and to make decisions. They used their symptoms to gain pity. An unhappy parental, and especially marital, situation applied to both. One escaped by excessive social activity, which undoubtedly contributed to her tuberculosis; the other, by being a chronic, whining complainer, who alienated all her friends and was unable for long periods to perform her duties as housewife and mother. Each patient, particularly the nontuberculous woman, projected her inadequacies on to others. The former accepted psychotherapy with some benefit; the latter refused it, and when last seen was unchanged emotionally.

Cases 3 and 3 A are those of young men who were under constant tension to live up to the unnecessarily strict demands of their parents. Both were idealistic, tense, and hostile to their mothers, and both escaped into intellectual achievement as their only means of self-expression. Feelings of inferiority were pronounced but suppressed. The tuberculous patient, who had been in bed five years, improved under streptomycin therapy, and then began to assert himself and learned to socialize. The other asserted himself by marrying at an early age but, not learning how to meet frustrations, flew into uncontrollable rages and had an unhappy sexual life. Fear of failure was traced to fear of displeasing his mother, and under psychotherapy he was able to adjust sexually and emotionally on a stable plane.

Cases 4 and 4 A illustrate strong domination and rejection by parents and husband. Physical, sexual, and financial hardships were prominent in childhood, and each patient rebelled by early marriage, which was unsuccessful. When tension became too great, there was a coincidental, probably causal, development of tuberculosis in the one case, and of drug addiction and agitation severe enough to require temporary hospitalization in the other.

Cases 5 and 5 A also illustrate marked rejection by one or both parents, with resultant withdrawal from social contacts, exaggerated sense of responsibility, desire for approval but feelings of inferiority, insecurity and timidity in seeking it, yet potentially sufficient ego strength to enable the patient to make a proper adjustment when given sympathetic guidance and affection.

It must, of course, be realized that in the cases in the A category tuberculosis might conceivably develop in the future. The patients have, however, been under severe emotional strain for long periods, and to date their pulmonary condition is normal. We feel that these cases indicate that there is no characteristic personality for patients with tuberculosis.

THERAPY

Therapy was flexible, depending on the particular needs of the patient and the time available. With most patients, analytically oriented brief psychotherapy was used, with the therapist taking an active part in interpretation and explanation. In a few patients, seen weekly for many months, deep probing was possible. In general, however, there was no opportunity for intensive deep therapy. A small number of patients were felt to require orthodox analysis, which, unfortunately, was not pos-

sible. Full use was made of rehabilitation facilities, including psychological testing and vocational aptitude tests. An active, psychiatrically trained social service department was of great assistance in guidance and, in some cases, in therapeutic management.

It is difficult to judge the value of psychiatric services on a wide scale. Almost all patients were definitely benefited, as judged by their own reactions and the opinion of the therapist. Many persons felt calmer and acquired more insight. We do not have follow-up studies, but patients discharged by the psychiatrist rarely asked for further help with emotional problems, nor were they considered by the resident physicians to require it. Perhaps the best criterion was found when the psychiatrist was absent for six months. The medical, nursing, social service, and administrative departments all indicated that a needed medical facility had been missing, and they were most anxious for renewal of psychiatric guidance for the patients.

SUMMARY

The psychiatric program in a 230-bed sanatorium for patients with pulmonary tuberculosis is outlined.

It is our opinion that there is no specific type of personality in patients who have pulmonary tuberculosis. Case histories of both tuberculous and nontuberculous patients are given in pairs. The psychodynamics vary widely; yet for each mechanism examples are found in both the tuberculous and the nontuberculous category.

Psychotherapy is a valuable adjunct in the care of patients with pulmonary tuberculosis.

5 Mamaroneck Road.

Dr. Alfred S. Dooneief, physician in charge, Montefiore Hospital Country Sanatorium, and Dr. Paul H. Hoch, principal research psychiatrist, New York State Psychiatric Institute and Hospital, gave helpful suggestions and criticism.

PSYCHOSIS OCCURRING DURING ANTABUSE® ADMINISTRATION

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PREVIOUS reports on the administration of tetraethylthiuramdisulfide (antabuse*) have listed various symptoms which commonly occur in patients who are taking the drug.¹ These symptoms have been found to be fatigue, headache, dizziness, gastrointestinal disturbances, skin allergies, unpleasant taste in the mouth and reduced sexual potency.

Psychosis also has been reported as a complication of tetraethylthiuramdisulfide therapy. Lemieux ² mentioned two patients in whom manic-like reactions developed. One patient's disturbance cleared after withdrawal of the drug; the other's, after reduction of the dose. Bennett, McKeever, and Turk, ³ in reporting six cases of psychosis complicating tetraethylthiuramdisulfide therapy, noted a predominant paranoid reaction in two and an expansive trend in one; discontinuance of the drug was necessary with five of the patients; but of these, all had evidence of hepatic damage, and four, symptoms of organic damage to the brain, prior to treatment with tetraethylthiuramdisulfide. Knutsen ⁴ reported the case of a patient with an anxiety neurosis who became confused and hallucinated while taking tetraethylthiuramdisulfide.

A case is reported in which a psychotic episode developed while the patient was under treatment with tetraethylthiuramdisulfide at the Cincinnati General Hospital. The drug was discontinued, with disappearance of symptoms. The patient's reaction to a second course of the drug, preceded by placebos, is reported.

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^{1.} Glud, E.: The Treatment of Alcoholic Patients in Denmark with "Antabuse®" with Suggestions for its Trial in the United States, Quart. Stud. Alcohol 10:185, 1949. Gelbman, F., and Epstein, H. B.: Initial Clinical Experience with Antabuse,® Canad. M. A. J. 60:549, 1949. Bell, R. G., and Smith, H. W.: Preliminary Report on Clinical Trials of Antabuse,® ibid. 60:286, 1949. Barrera, S. E.; Osinski, W. A., and Davidoff, E.: The Use of Antabuse® (Tetraethylthiuramdisulphide) in Chronic Alcoholics, Am. J. Psychiat. 107:8, 1950.

^{2.} Lemieux, L. H.: L'alcoolisme chronique et ses traitements, Laval méd. 14:1304, 1949.

^{3.} Bennett, A. E.; McKeever, L. G., and Turk, R. E.: Psychotic Reactions During Tetraethylthiuramdisulfide (Antabuse*) Therapy, J. A. M. A. 145:483 (Feb. 17) 1951.

Knutsen, B.: Komplikasjoner ved antabus*-behandling, Tidsskr. norske lægefor. 69:436, 1949.

REPORT OF CASE

History.-J. O., a white married man aged 45, a commercial agent and accountant, was referred by the local chapter of Alcoholics Anonymous. He stated that he had been a chronic alcoholic for nearly 20 yr. and that during the past seven to eight years his drinking had been becoming more serious. His drinking sprees were two to three days long and occurred almost every week. The sprees were usually preceded by "tension," and the drinking was done to relieve this. The sprees almost always resulted in intoxication with amnesia.

On two occasions, in 1947 and 1949, the patient reported that he had had a brief episode of delirium tremens. Each episode lasted only one night. The longest period of sobriety experienced by the patient was seven weeks, and this was seven years ago. Subsequently, he had been an irregular member of Alcoholics Anonymous.

The patient's work record was better than is usual with an alcoholic history such as his. He had held several very responsible positions but had gradually drifted downward. Nevertheless, at the time of admission he was commercial agent for a trucking firm and did accounting on the side.

The patient expressed a strong desire to rid himself of alcoholism by trying tetraethylthiuramdisulfide. He stated that he had taken a "couple drinks" three days prior to admission.

Initial Study.—Physical examination revealed nothing unusual except for his short stature. His height was 5 ft. 3 in. (160 cm.).

Laboratory examinations gave normal results. These included electrocardiographic and roentgenographic studies, urinalysis, determinations of kidney and liver function (including the bromsulfalein test), glucose tolerance test, differential blood count, Kahn test of the blood, and determinations of the urea nitrogen level. An electroencephalogram was also obtained and found to be normal both in the sleeping and in the waking state.

Psychiatric examination revealed no abnormalities of mood, ideation, or sensorial function. The appearance and behavior were adequate.

Additional History: The patient, the oldest of three siblings, had two brothers, six and eight years younger than he. His father and mother were still living and well. The mother was described as a tectotaler, old-fashioned, frugal, and strict. The father was the patient's favorite and was described as understanding, lenient, good-natured, and a spendthrift; he was alcoholic until the age of 42, and the patient recalled drunken stag parties given by the father in their home. The patient stated that he and his brothers had always borne considerable resentment toward the parents. The reason given was that they were dissatisfied with their parents' clinging to "old-fashioned ways." At the time of his admission the patient was seeing the parents only once a month, though he lived in the same neighborhood. The patient's earliest memory was at the age of 7 yr., when his parents had a candy store and he had to get up early in the morning to deliver rolls and bread for them. The patient's two brothers were also chronic alcoholics, the older brother being the most severely affected. The patient married at the age of 25. He had two children, aged 17 and 6 yr. He described his wife as kind and considerate. Five years prior to his admission she divorced him because of his alcoholism but remarried him two years later.

Psychological Examinations (Rorschach and Thematic Apperception Test): The patient's good intelligence rating was confirmed. No psychotic reaction was manifested in these performances. Reality testing was intact. The patient's attitude was one of cautiousness and oversubmissiveness, as a reaction to strong unconscious hostile impulses. However, guilt toward this hostility, as well as fear of retribution, caused the patient to suppress his impulses and turn them on himself, resulting in self-destructive behavior.

Course in the Hospital.—The patient was admitted to Cincinnati General Hospital on May 1, 1950, and tetraethylthiuramdisulfide therapy was started on May 4. The usual procedure in administering the drug 5 was followed; this consists in giving the patient 2 gm. of tetraethylthiuramdisulfide the first day, 1.5 gm. the second day, 1 gm. the third day, and 0.75 gm. daily thereafter.

Footnote 1. Knutsen.⁴

On May 8 (fifth day of therapy) the patient suddenly experienced onset of anorexia, headache, epigastric distress, constipation, fatigue, vertigo, and sensorial clouding. Physical examination revealed nothing remarkable except for a slight increase in the pulse rate. Search for a history of recent ingestion of alcohol-containing substances was nonproductive except for his having had the "couple drinks" three days prior to admission.

Tetraethylthiuramdisulfide administration was omitted on May 8 and 9. The patient gradually improved during these two days under treatment with acetylsalicylic acid, laxatives, and bed rest. Tetraethylthiuramdisulfide therapy was resumed on May 10, with a dose of 0.75 gm. The patient experienced no further symptoms of this kind, though mild fatigue remained.

He was given his first challenge dose of 1 oz. (30 cc.) of whisky on May 12. He experienced a typical moderate reaction 6; five minutes after the ingestion of alcohol the patient said that he "felt sunburned all over." Shortly thereafter he complained of palpitation, dyspnea, headache and blurred vision. His pulse rate increased to 126 per minute, while the respiration rate was 30 per minute. The blood pressure fell slightly, and the scleral vessels were dilated. Although he complained of nausea, he did not vomit. On the morning of May 15 the patient was given his second challenge dose of 1 oz. of whisky. He experienced a similar reaction to this dose, but complained also of confusion. However, all symptoms had cleared within approximately 30 min. except for headache, which persisted two hours longer.

The patient was discharged at 6 p. m. on the evening of May 15. He was in excellent spirits and professed enthusiasm about the tetraethylthiuramdisulfide treatment. He was placed on a maintenance dose of 0.5 gm. of the drug daily and was given an appointment to come to

the clinic two weeks later.

Behavior After Discharge.—The patient began to experience difficulty as soon as he left the hospital, but he and his wife allowed this to continue for five days before notifying his physician. By this time the patient had discontinued use of tetraethylthiuramdisulfide, and his difficulties were clearing. Three days later, when the patient finally came to the clinic, his symptoms had cleared completely. The details of his condition and behavior during the abnormal period were obtained from a retrospective day-by-day account of the five days involved, prepared by the patient and his wife. Excerpts from this account follow.

"May 15: Returned from hospital. Unable to concentrate. Objects seemed unreal. Semistupor. Took antabuse* tablet [0.5 gm.]. To bed at 9 p. m. Attempted intercourse from 9 to 12 p. m., finally reaching orgasm, with resulting cracking sensation through center of brain. Dreamed that night of attending hotel affair as a moneyed man, spreading gifts and putting on a big-shot attitude. Accompanied by wife, who was puzzled. Wife reminded me after return from party that I had written a bogus check for \$61,000 to put on this act.

"May 16: Fatigued. Couldn't get to office until noon. Overly talkative. Couldn't concentrate on work. Drove home in exhausted state, bouncing off curbs. Ate heartily. Took antabuse® and retired early. Attempted intercourse four and one-half hours, without success.

"May 17: Fatigued. Arrived at office at 10 a. m. Confused. Couldn't do simple calculations. Left office for rest and too sleepy to return in afternoon. Drove home. Played with penis like a kid. No appetite. Took antabuse,* retired early, and slept soundly. No attempt at intercourse.

"May 18: To office by 9 a. m. Split personality feelings. Couldn't do ordinary problems. Fatigued. Slept at desk from 2 until 4:45 p. m. Umpired baseball game at 6:30 p. m. On several occasions, jumped call on the batter from one to three strikes and was difficult to convince of error. Took antabuse* and retired early, completely fatigued.

"May 19: Arrived at office at 8:30 a.m. Couldn't begin to balance books. Tried to bluff. Employer told me not to come in next morning, as I had written bad checks and made advances toward his pregnant daughter. Realized shouldn't take antabuse[®] that night and didn't.

"May 20: At 4 a. m. awoke to realization had been under influence of drug and was just coming out of it with clear sense. By noon drug wearing off. Fatigued but symptoms clearing."

Hald, J., and Jacobsen, E.: A Drug Sensitizing the Organism to Ethyl Alcohol, Lancet 2:1001, 1948.

The patient had seen the therapist on May 18 and had mentioned that he was fatigued and somewhat confused. However, he did not speak of the other symptoms, mentioned above. He was scheduled to come in May 30, but it was suggested that instead he come on May 23. He appeared in the clinic on the evening of May 23 and stated that he had discontinued the medication as of May 19. He pointed out that he was "ruining himself" and submitted the above day-by-day account. He professed having a vague memory for some of the happenings noted, but stated that he had complete amnesia for most of them. He was gay and jaunty, free of sensorial clouding, and had apparently returned to his normal self. He agreed to the suggestion that he return at weekly intervals. However, he did not keep this agreement, and subsequent attempts to get in contact with him were fruitless. His employer said the patient had been fired. Several attempts were made to reach the patient by telephone, but there was no answer. Finally, the patient consulted the therapist on July 5. He had returned to his former position.

He was seen again on July 10, 1950. He was obviously under the influence of alcohol; he said that he had not been drinking until June 14 because of fear of the tetraethylthiuramdisulfide reaction, but he had been drinking almost continuously since and was desperate for help. After this, he maintained infrequent contact with the clinic. Prior to two of his appointments, he telephoned from a bar, pointing out how worthless he was and apologizing for not being able to come in. During this period, he had lost his job, been separated from his wife, lost his driver's license through suspension and been forced to sell his car.

We were interested in attempting to reinstate the tetraethylthiuramdisulfide regimen, so that it might be observed whether the patient would experience the same symptoms as before and, if so, whether he could be maintained symptom-free on a smaller, but still effective, dose. We were also interested in finding out whether or not the patient would experience his previous symptoms on a course of placebos. This investigation could not be conducted in the hospital, as the patient was unable to leave his work. Accordingly, it was arranged that he see his therapist every other day and report by phone on the intervening days.

On Aug. 30 the patient was seen after a three day period of sobriety. When it was suggested that another trial of tetraethylthiuramdisulfide seemed advisable, he immediately refused, but very shortly thereafter agreed. Accordingly, he was given a placebo. He took placebos for the following 13 days, and on two of these days he took two and three placebos daily. During this 13 day period he complained once of mild fatigue and gastric distress. Several times he commented that he had thought of drinking but refrained from doing so only because of the fear of the tetraethylthiuramdisulfide reaction. Once, in a joking manner, he asked whether he was really receiving the drug. On Sept. 12 a careful sensorial examination revealed nothing of significance. At that time, administration of tetraethylthiuramdisulfide was resumed, beginning with 4 tablets (2 gm.) a day and reducing to 1 tablet (0.5 gm.) a day. On Sept. 14 the patient began complaining of severe fatigue. It was the impression of the therapist that he was overdramatizing some of his symptoms. He said he had a lightheaded feeling and was doing everything mechanically. "I'm unable to concentrate. Food tastes like paste, and I have no appetite. I've been getting dizzy. I don't see how I can continue to take the medicine. I'm going to lose my job." He said he could not tolerate seeing his memory suffer so badly. At this time a thorough examination of the mental status, including the sensorium, was made. No abnormality was found. He was persuaded to continue the use of 1 tablet of tetraethylthiuramdisulfide a day, and an electroencephalogram was secured the following morning: this tracing was essentially normal. However, when he came in two days later, even more upset and dramatic than before, he was told to reduce the dose of the drug to ½ tablet (0.25 gm.) daily. The patient submitted the following résumé of his past few days:

"Aug. 31: Started taking a single tablet dose daily of antabuse® [actually placebos]. No reaction of any kind.

"Saturday, Sept. 9: Terrific desire to drink, but afraid of possible antabuse® effect. After I had spent three hours in theater, feeling left me, and I was in better spirits when I got home.

"Monday, Sept. 11: Began noticing fatigue symptoms, appearing in afternoon. Feel just about able to finish day's work, eat and go to bed. No desire to read or work in evening.

"Tuesday and Wednesday, Sept. 12 and 13: Fatigue slightly greater; more tired at end of day. Able to do nothing but go to bed after supper. Cold in head and cough may be making me worse.

"Tuesday night, Sept. 12: Four antabuse® tablets [real antabuse® therapy begun]. No undue symptoms until Wednesday evening. Supposed to umpire two ball games but, on arriving at first one, at 7 p. m., began to have dizzy spells, stomach upset and terriffic desire just to lie down. Luckily, ball game was called off on account of wet grounds; so I walked 1½ miles home, with lightheaded feeling and sick stomach. Exhausted when I got home; no desire for supper, which I had skipped earlier. Just a taste of food and to bed. Restless night.

"Wednesday night, Sept. 13: Took 3 tablets. Dreamed all night. Restless. No appetite all day Thursday. Logy, unable to concentrate on new work. Couldn't remember what transpired during day. Unable to recount in the evening what work I had done through the day. Everything seemed mechanical, with no real forethought. Hope I did new work correctly. To hospital in evening—extremely fatigued—took 2 tablets. Home and to bed at 10:30 p. m., completely exhausted.

Friday, Sept. 15: At hospital for electroencephalographic test at 8 a. m. Tired, felt as though had no sleep last night, although had a fairly quiet night, only waking twice—disturbed with dreams. Day same as Thursday, everything mechanical—unable to concentrate; all food tastes like paste; no appetite; headache and dizziness. Miserable day, with fatigue coming on about 3 p. m. Took vitamin C pills but not sure they helped any. Finally home (6 p. m.); a little food and a hot bath seemed to perk me up a bit. Decided on intercourse with my wife, and it resulted in a rather long-drawn-out session, much slower on climax than usual, with thoughts of possibly not being able to come to a climax. Left an ache in prostate region, carried over into Saturday. Asleep at 9:30 p. m. after 1 tablet. More restful night, only waking once.

"Saturday, Sept. 16: Woke up tired, but appetite slightly better, and ate a little more than usual. Day about the same as Friday—mechanical and unable to concentrate clearly. Made mistakes in typing. Loose, lightheaded feeling; tired; only 1 tablet taken today at noon."

The dose of tetraethylthiuramdisulfide was reduced from 0.5 to 0.125 gm. at this point (Sept. 16), when it was feared that the patient was heading toward another psychotic break. Subsequently, he has been maintained on the daily dose of 0.125 gm. On Sept. 25 he was given a "challenge" dose (1 oz.) of whisky. He had a mild to moderate reaction, with flushing of the face, increase in pulse rate to 96 per minute and vague gastrointestinal distress with considerable eructation. Interestingly, an hour after this reaction the patient had another reaction, which was very similar. The patient continued with the treatment and for several weeks complained of moderate fatigue, "pasty" taste to foods and decreased sexual potency. These symptoms gradually diminished, and on the date of this report (Feb. 10, 1951) the patient is free from symptoms. He is now making a good adjustment, has received several promotions, has become reconciled with his wife, and is partaking of new social activities.

We have treated 24 other patients with tetraethylthiuramdisulfide. Of these, two experienced similar, but less severe, reactions than did this patient. These patients also responded readily to a reduced dose of tetraethylthiuramdisulfide.

SUMMARY

A case of psychosis occurring during the administration of tetraethylthiuramdisulfide (antabuse[®]) is reported.

The psychotic symptoms subsided coincident with reduction of the dose of tetraethylthiuramdisulfide.

This case reemphasizes the desirability of arriving at the minimal optimal dose for each patient. This procedure may involve initial failure and necessitate considerable manipulation of the dose, as well as frequent contacts with the physician. The clinical picture in this case, based primarily on the patient's subjective complaints and work performance, would seem to support the presumptive diagnosis of a toxic reaction to tetraethylthiuramdisulfide. Before the second course of the drug, a course of placebo treatment was given, with no appreciable production of symptoms. During the second course of tetraethylthiuramdisulfide, when the patient was near the peak of his subjective complaints, a thorough sensorial examination, followed by an electroencephalographic study, revealed nothing suggestive of drug intoxication.

We can offer no explanation of the discrepancy, except to speculate on the possibility of a toxic mental state having developed which could not be detected by the routine measures of sensorial examination and electroencephalography. It is anticipated that as use of tetraethylthiuramdisulfide is extended, similar clinical pictures will be reported.

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PSYCHOLOGICAL STUDIES ON PATIENTS WITH MULTIPLE SCLEROSIS

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In A RECENT publication one of us (M.H.) has reported briefly on psychological testing of 61 patients with multiple sclerosis. In this study there were used as controls patients equally handicapped physically with tabes, poliomyelitis or Parkinsonism ; persons with neurotic and psychosomatic difficulties, and persons free from symptoms at the time of testing, designated for the sake of simplicity as "normal."

Summarizing the findings from this previous study, we may say that while no typical stereotyped or uniform personality picture of the patients with multiple sclerosis emerged, such as has been found by several investigators in cases of brain damage, nonetheless in every test used there were some items which differentiated this experimental group from the controls. Expressed in general terms, these findings could be epitomized as showing in the multiple sclerosis patients an overemphasis of dependency needs, a virtually complete absence of body-centered anxiety, a minimum of inner conflict or an attitude of resignation and an unrealistic tendency to see the world through rose-colored glasses.

It is important to emphasize here that the discovery of certain trends in the group as a whole does not mean that every patient in the multiple sclerosis group showed these characteristics. It is only that the incidence of these traits is significantly higher in this group than in the control groups. Individual multiple sclerosis patients deviated markedly from the general pattern, some giving no indication of the characteristic constellation of the findings.

At the conclusion of the previous study,¹ we were left with the question whether persons possessing such traits could, for some reason, be more subject to that particular disease or whether the actual conditions of the disease itself evoked, fostered and developed attitudes which then became crystallized and were demonstrable in the test findings. That psychological states introduce demonstrable physiological changes has, of course, been shown by several investigators, notably

Harrower, M. R.: Results of Psychometric and Personality Tests in Multiple Sclerosis, A. Res. Nerv. & Ment. Dis. Proc. (1948) 28:461-470, 1950.

Dr. Gotthard Booth permitted us to study the Rorschach records which he has taken on Parkinsonian patients.

^{3. (}a) Piotrowski, Z.: The Rorschach Inkblot Method in Organic Disturbances of the Central Nervous System, J. Nerv. & Ment. Dis. 86:525-537 (Nov.) 1937. (b) Harrower-Erickson, M. R.: Personality Changes Accompanying Cerebral Lesions: Rorschach Studies of Patients with Cerebral Tumors, Arch. Neurol. & Psychiat. 43:859-890 (May) 1940.

Wolf, Wolff and Mittelman.⁴ As the most recent, we may cite Graham.⁵ His paper shows that "a conscious feeling of anxiety, tension, or hostility is associated with increased minute vessel tone and constriction of small arteries. These are the changes seen in the persons with cold, sweaty palms and in an extreme form in Raynaud's disease. . . . A second pattern involves situations associated with conscious feelings of resentment without hostility, and as a result minute vessels lose tone and small arteries dilate. . . . These are the changes of urticaria and eczema."⁵

PRESENT INVESTIGATION

The study to be reported here attempted to throw further light on this question. Our number of multiple sclerosis subjects was increased to 140, and a more complete breakdown within the group was attempted. We considered separately (1) patients who at the time of testing demonstrated a remission of symptoms; (2)

TABLE 1 .- Age Ranges of Patients with Multiple Sclerosis and of the Control Patients

Age	Range, Yr.	Age	Range, Yr.
Multiple sclerosis	18-76	Parkinson's disease	22-62
Poliomyelitis	17-46	"Normal" patients	18-64
Tabes	48-75	Neurotic patients	18-61

TABLE 2.—Sex Distribution of Patients with Multiple Sclerosis and of Control Subjects

Groups Studied	Total	Male	Female
Multiple sclerosis	144	67	77
Remission	14	3	11
Mild	28	1ā	18
Mild and advanced (Kaiser-Kabat Institute)	34	14	20
Advanced (home bound)	27	9	18
Advanced (hospitalized)	41	26	15
Poliomyelitis	21	11	10
Tabes	20	14	6
Parkinson's disease	49	26	23
Neurotle subjects *	200	100	100
Families	20	9	11

^{*} Since many records of persons with neurotic difficulties were available to us, it was possible here to choose an equal number of makes and females. In the other groups no systematic attempt was made to have equal numbers of men and women, as this seemed to be a relatively unimportant orientation.

patients with mild disease, who were not as yet handicapped by the disease; (3) patients who were severely ill and living in their own homes; (4) patients who were severely ill and hospitalized, and, finally, (5) a group of patients at the Kaiser-Kabat Institute, for the purpose of discovering whether an environment aimed at fostering independence would modify the characteristic overemphasis on dependency needs which had been shown as characteristic of the group as a whole.

A further feature of this study included the examination of husbands, wives and close relatives of a number of patients. This group, with backgrounds, educational

^{4.} Wolf, S., and Wolff, H. G.: Evidence on Genesis of Peptic Ulcer in Man, J. A. M. A. 120:670-675 (Oct. 31) 1942. Mittelman, B., and Wolff, H. G.: Emotions and Gastroduodenal Function: Experimental Studies on Patients with Gastritis, Duodenitis and Peptic Ulcer, Psychosom. Med. 4:5-61 (Jan.) 1942.

^{5.} Graham, D. T.: Life Situations, Cutaneous Vascular Reactions and Skin Disease, read before the American Psychosomatic Society, April 1950.

opportunities and financial status identical with those of the patients in question, form a control group to take its place among the others with which comparisons are made.

The age range of our patients and control subjects is recorded in table 1.

Table 2 shows the sex distribution of the patients and the control groups. Table 3 shows the distribution of the occupations and professions of our patients,

Needless to say, we are not suggesting that multiple sclerosis is an "occupational disease," but in view of the strong dependency findings, it might have been argued that these patients previously would have been found in professions lacking in self assertiveness and initiative. This, however, does not appear to be true. In this connection, it is interesting to compare the statement of Dr. Gotthard Booth in regard to his Parkinsonian patients. He expressed the belief that the professions from which his Parkinsonian patients came indicated "a marked impulse toward action." However, many of the professions listed here for multiple sclerosis patients are the same as those found by Booth for Parkinsonian patients.

TABLE 3 .- Distribution of Professions and Occupations of Patients with Multiple Sclerosis

Males	Females
Salesman Clerk Clerk Craftsman Teacher Student Coal miner Truck driver Farmer Woodcutter Physician Butcher Artist Pharmacist Waiter Priest (Roman Catholie) (Episcopalian) Druggist Gardener Total	14 Housewife 14 Clerk 11 Saleswoman 4 Nurse 4 Teacher 4 Milliner 3 Model 2 Artist Nun Nun 1 Hairdresser 1 Musician 1 Farmer 1 Total

The test battery given to our initial 61 patients included the verbal Wechsler-Bellevue intelligence scale, the Rorschach test, evaluated both for its formal characteristics and for its descriptive, qualitative features; the Szondi test; the Man-Woman Drawings, and the Most Unpleasant Concept test.^a These tests were repeated in our further studies.

We shall now consider the findings from each of these tests independently, commenting on the characteristics shown by the group as a whole and on those which emerged as specific to our patients in the various subgroups.

The Verbal Wechsler-Bellevue Scale.—Tables 4, 5 and 6 epitomize our findings with the verbal Wechsler-Bellevue intelligence scales. They are of interest because of the similar trend which emerges, despite the fact that they reflect three ways of appraising the material.

Table 4 shows all our subjects divided in terms of very superior and superior ratings, as opposed to those of high average and average ratings. The multiple

The Most Unpleasant Concept Test was developed by one of us (M. H.). It has been reported in detail elsewhere (The Most Unpleasant Concept Test, J. Clin. Psychol. 6:213-233 [July] 1950).

sclerosis patients are arranged in terms of the severity of the disease, from the group in remission to the patients with advanced disease who are hospitalized. It will be noticed that the percentage of very superior and superior ratings decreases from the patients in remission to those with mild disease, to the group that is composed of patients with mild and advanced disease, making a sharp drop when the subgroup is composed only of patients with advanced disease, regardless of whether they are home bound or hospitalized.

At the other end of the scale, one finds that persons with acute neurotic difficulties show an extremely high percentage of patients with very superior and superior ratings, whereas none of the patients with tabes appear in this group.

TABLE 4.—Distribution of Intelligence Quotients

Groups Studied	Group with Very Superior and Superior Ratings, %	Group with High Average and Average Ratings, %
Multiple scierosis		
Remission	. 36	64
Mild	22	78
Mild and advanced (K. K. Institute)	18	82
Advanced (home bound)	. 4	96
Advanced (hospitalized)	. 7	93
Poliomyelitis	16	84
Tabes	. 0	100
Neurotic persons	65	35

TABLE 5 .- Percentage of Cases with Marked Scatter (7 Points and Over) on Wechsler-Bellevue Scale

	Per Cent		Per Cent
Multiple sclerosis		Poliomyelitis	23
Remission	7	Tabes	
Mild	16	Neurotic persons	39
Mild and advanced (K. K. Institute)	28	Families	20
Advanced (home bound)	33		
Advanced (hospitalized)	38	*	

Viewed from a different standpoint, table 5 expresses the percentage of cases in which marked scatter or acute irregularity or erraticness of performance was noted. Here, again, the same progression is found. The percentage of cases with marked scatter is the lowest in the remission group and highest in the advanced hospitalized group. In our control groups, an equally high percentage of subjects with neurotic difficulties show this erratic performance, as is true also of the tabetic patients. With the neurotic group, therefore, one has high intelligence and an errationess of performance, and with the tabetic group, low intelligence and much erraticness, making, of course, an entirely different total picture.

If one takes the members of the families of the multiple sclerosis patients as constituting some arbitrary frame of reference, one finds that 20 per cent of such persons may show this extreme scatter. Multiple sclerosis patients in remission and those with only mild forms of the disease are shown to have fewer cases with much scatter, whereas patients with the more advanced disease show increased incidence of this characteristic of the group.

Table 6 shows a consistent finding among all multiple sclerosis patients; namely, if one estimates the performance on the test as a whole in terms of the subtests most likely to be best, as opposed to least, well performed, one finds consistent indication of poor memory in the multiple sclerosis patients, regardless of the subgroup to which the patients belong. The digit span test is the one most poorly performed in all multiple sclerosis groups. In all but one of the various subgroups the information test is most likely to be performed the best.

Among all control groups, only the tabetic patients show the pattern of memory as the most severely impaired.

Summarizing these findings, we may say that as the disease progresses a greater amount of scatter among the subtest scores, i. e., a less well integrated intellectual performance, appears. In the same way, there is a decrease in the percentage of the multiple sclerosis group which falls within the very superior and superior ratings as the disease advances. From a breakdown of the findings for all subgroups of multiple sclerosis patients, it appears that memory is the most vulnerable trait examined in the subtests.

TABLE 6.—Distribution of Subtest Scores on the Wechsler-Bellevue Scale

Groups Studied	Most Frequently Found as Highest Subtest Score	Most Frequently Found as Lowest Subtest Score
Multiple sclerosis		
Remission	Similarities	Digit span
Mild	Information	Digit span
Mild and advanced (K. K. Institute)	Information	Digit span
Advanced (home bound)	Information	Digit span
Advanced (hospitalized)	Information	Digit span
Poliomyelitis	Comprehension and digit span	Arithmetic
Tabes	Comprehension	Digit span
Neurotic patients	Information	Comprehension
Families	Information	Similarities

The Rorschach Test.—Data from the Rorschach test can best be epitomized under negative and positive findings.

Negative Findings: For only four of the 140 patients examined was a "typical" organic personality record found, such as has been described as characteristic of persons with cerebral lesions by Piotrowski ^{3a} and Harrower. ^{3b}

This conclusion has also been reached by Dr. Samuel Beck, as reported by Grinker. Beck states that "the signs of organic brain disease, such as excessive self-criticism, uncertainty, low productivity, retardation of response time, deviation from accuracy, perseveration, and confabulation were quantitatively less than in proven cases of brain disease."⁷

We would also list as a negative finding absence of so-called color shock, which Rorschach isolated as particularly characteristic of neurotic difficulties. Expressed in general terms, "color shock" means that, given in the test an opportunity to liberate emotions, the subject responds in the opposite way, namely, by being, metaphorically, set back on his heels, blocked, inhibited, unable to give vent to his repressed emotions. Since Rorschach's initial findings, over 20 years ago, color

^{7.} Grinker, R. R.; Ham, G. C., and Robbins, F. P.: Some Psychodynamic Factors in Multiple Sclerosis, A. Res. Nerv. & Ment. Dis., Proc. (1948) 28:456-460, 1950.

shock has remained one of the primary indications of neurotic disturbance. Absence of this as a characteristic of multiple sclerosis records as a whole is thereby of importance in differential diagnosis (hysteria).

This is not to say that no person with multiple sclerosis showed emotional disturbance: rather, it is not characteristic of the group as a whole to manifest emotional disturbance in this way.

Positive Findings: As can be seen from table 7, no one personality type, no one "experience-balance" characterizes the multiple sclerosis patients.

In order to make this statement more meaningful, a brief discussion of Rorschach's "experience-balance" may be in order. This is a fundamental concept of the Rorschach test, relating to the extent to which the subject lives within his own private psychic world or, on the contrary, derives stimulation and satisfaction predominantly from extroverted living. Rorschach distinguished four main types of persons, with innumerable subdivisions and gradations. These four types are (1) the coarctated, i.e., the person with relatively stereotyped modes of reaction who has developed neither a rich inner life of fantasy nor the capacity to lead a

TABLE 7 .- Distribution of Personality Types *

	Intro- verted, %	Extro- verted, %	Ambi- equal, %	Coare- tative, %	Coarc- tated, %
Multiple sclerosis					
Remission	7	3.4	57	7	14
Mild	21	11	7	50	11
Mild and advanced (K. K. Institute)		36	18	24	6
Advanced (home bound)	15	27	8	42	8
Advanced (hospitalized)	13	5	10	43	30
Tabes	6	44	0	39	11
Poliomyelitis		20	12	36	16
Parkinson's disease	. 13	24	7	20	35
Families	. 5	32	36	9	18
Neurotic patients					

satisfactory life in terms of emotional rapport with others; (2) the introversive, the person primarily interested in his own private psychic world of fantasy and ideas; (3) the extrotensive, the practical, outgoing extrovert, and (4) the "ambiequal," the person capable of living both within his own psychic universe and in the world of reality, as a person of action. A breakdown of our cases shows that all such types are represented.

We may begin by consideration of those patients in the ambiequal group, the group representing those patients with the richest and most expanded type of personality, the persons with the widest range of psychic reactivity. Here we find that the two highest scores occur in the families which we may take as our "normal" controls, and even more strikingly in patients with multiple sclerosis during a period of remission. Together with the feeling of well-being, then, the personality literally expands and has a greater capacity for psychological experience. All other scores, with the limited exception of those for the patients with mild and advanced disease at the Kaiser-Kabat Institute, are of a different order of magnitude. Not a single tabetic patient, for example, is characterized by his personality structure.

We may now consider the coarctated personality type, or the most restricted and stereotyped. In this connection, we have introduced a fifth category, the coarctative, which is indicative of those personalities slightly less constricted than the extreme type. These two groups may best be considered together, and for that purpose table 8 has been constructed. If we contrast the three personality types which are the richest with the two which indicate considerable stereotypy and poverty of personality structure, we find an interesting grouping in which the distribution found in patients in remission, among the "control" families and among the Kaiser-Kabat Institute patients, where emphasis has been on a constructive attempt to deal with the disease, shows a much higher percentage of expanded personality types than is found elsewhere. The most constricted picture is found in the hospitalized patients with advanced disease, and the next, among the patients with mild disease.

An additional finding of interest relates to the distribution of anatomical answers in patients with multiple sclerosis and, as it turns out, with other organic

TABLE 8.-Comparison of Expanded and Constricted Personality Types

	Expanded, %	Constricted, %
Remission	78	22
Families	73	27
K. K. Institute	70	30
Tabes	50	50
Advanced (home bound)	50	50
Poliomyelitis	50	50
Parkinson's disease	43	54
Mild	39	61
Advanced (hospitalized)	27	73

TABLE 9.—Answers Reflecting Anxiety and Concern Over Bodily Functions (Rorschach Test)

No. of Patients	Disease Group	Answers per Person
61	Multiple selerosis	0.5
21	Poliomyelitis	1.0
49	Parkinsonism	1.4
	"Normals"	
200 (10 subgroups)	Emotionally disturbed patients-neurotic and psychosomatic disorders	3.1.,.,.5.

diseases as well, when compared with the emotionally disturbed and the normal controls. Table 9 epitomizes these findings.

Table 10 shows an additional breakdown in terms of the multiple sclerosis subgroups. Tables 9 and 10 show that when these figures, are compared with the findings for 10 or 12 groups of "normal" subjects and an equal number of groups of persons emotionally disturbed the number of anatomical answers given by multiple sclerosis patients is significantly less. This, however, does not pertain to multiple sclerosis patients alone. There is a similar finding for the tabetic patients and, although to a slightly less degree, for those with poliomyelitis and Parkinsonism. We are forced to the conclusion, therefore, that these disease groups show an absence, a positive lack, of anatomical answers, a response found to some degree in symptom-free persons and clearly overemphasized in patients who are emotionally disturbed. It is also interesting to note that the patients with remissions most nearly approximate the normal distribution, with a score of 1.4, while the

families of the multiple sclerosis patients, considered as an independent normal group, fall within the range of other normal subjects, i.e., 1.75.

Rorschach himself considered the anatomical answers as indicative of some intellectual strivings on the part of the person tested. While this is not the place to discuss this hypothesis, it is clear from extensive records of later investigators that anatomical answers are in some way at least related to the subject's conscious or unconscious concern and anxiety over various bodily functions. For example, concern with the pelvis, when seen in the records of neurotic subjects, almost invariably masks a specific sexual anxiety, which can be elicited by other means. Other organs of the body can, by displacement, signify the pelvic region for the patient.

Moreover, among normal, symptom-free subjects one finds that anatomical answers may appear on certain occasions, after, let us say, an appendectomy, or even a bad cold at the time of testing. On a retest, these answers may be absent from the record.

What is strange, therefore, is that with extraordinary uniformity the multiple sclerosis patients and, to a certain degree, others similarly handicapped refuse to

Table 10.—Average Number of Anatomical Answers per Person

Group	Average No.
Previous assessment for 61 undifferentiated multiple sclerosis patients	. 0.5
Remission	. 1.4
Mild	. 0.79
Mild and advanced (K. K. Institute)	. 0.71
Advanced (home bound)	. 0.48
Advanced (hospitalized)	. 0.38
Families	. 1.75

be concerned with their bodily handicaps. One might say that the best type of adaptation to a disease situation for which there is no solution is actually to disregard its presence. Patients during a period of remission, on the other hand, who are coming back within the normal framework, may permit themselves some concern with the body.

Another consistent finding among our multiple sclerosis patients relates to an unexpected or unusual failure or rejection of one part of one of the ink blots. On Rorschach card VIII there is an area of the blot so segregated and so formed that it is practically impossible perceptually to overlook it as an entity, and its construction is so similar to some animal form that it would be safe to say that 99 per cent of all persons tested can respond to it. Among patients with brain tumors, for example, shortly after operation, when only the most undifferentiated type of psychological functioning is possible, this single response survived, even though most others were unobtainable. Table 11 shows the number of failures to this area of the blot which were obtained in the various subgroups of the multiple sclerosis patients.

The reason for this may be somewhat as follows: Many investigators have felt that this particular part of the blot allows, by the choice of animal and the type of action in which it is seen, for the subject somehow to epitomize himself as he sees himself or as he wishes to be. He may also express certain latent characteristics which, while not manifest in behavior, are nonetheless important dynamic components of the total personality. What makes the Rorschach record difficult of interpretation in many cases is that we do not yet have a distinguishing characteristic in terms of when such symbolism represents manifest or latent characteristics. One finds, for example, such things as "a timorous sheep hesitant to jump over a hurdle" in the record of a man hesitant about taking the final step toward marriage. Or one will find, again to this same area of the blot, such a response as "a porcupine with quills sticking out to defend himself from the attack of others," given by a subject whose bristling hostility keeps others at arm's length. One can also find such a response as "a sloth taking it easy" in the record of an unusually active subject. Here, one would say, the experienced need to combine relaxation with activity is registered.

TABLE 11.-Failures to Area of Blot on Rorschach Card VIII

Multiple sclerosis	Failure	Cold- Blooded	Warm- Blooded
Remissions	0	23	77
Mild	14	7	79
Mild and advanced (K. K. Institute)	14	7	79
Advanced (home bound)	15	7.5	77.5
Advanced (hospitalized)	22	2.5	75.5
Poliomyelitis	0	0	100
Tabes	0	0	100
Neurotic patients	0	3	97
Families	0	0	100

Booth was the first to draw our attention to this, as the following quotation shows:

- 1. Animal responses are determined by biological characteristics of the animal which are related to some dynamic aspect of the patient. Such responses may be motivated by intuitive rather than rational knowledge. Specific examples of such responses are:
 - (a) Cold-blooded animals-general functional dependence on the environment.
 - (b) Warm-blooded animals-general functional independence from the environment.
 - (c) Pig-tendency toward sustained muscular efforts.
 - (d) Sheep and cow-tendency toward group adjustment.
 - (e) Beasts of prey-destructive, aggressive tendencies.
 - "(f) Spider, scorpion and praying mantis-destructively possessive aspects of femininity.
 - 2. Animal responses are based on symbolic interpretation of animal behavior:
 - (a) Eagle-tendency toward individual freedom and self-assertion.
 - (b) Water birds—tendency toward spiritual, religious aspiration (according to findings in a group of 60 persons professionally engaged in church work).8

Characteristic, then, of our multiple sclerosis patients is a tendency to avoid identification in this way. When such identification occurs, there appears a higher proportion of answers of cold-blooded animals and fish than is found for the normal or control groups,

^{8.} Booth, G.: Organ Function and Form Perception: Use of Rorschach Method with Cases of Chronic Arthritis, Parkinsonism and Arterial Hypertension, Psychosom, Med. 8:367-385 (Nov.-Dec.) 1946.

One other, minor, finding is of interest as a clue for future research, although not followed up extensively here. Members of the same family, although tested separately, show a strong tendency to identify with the same animal. In one instance five members of the same family chose a highly unusual answer: a hyena. This response occurs only once in an unselected group of over 300 subjects.

Szondi Test.-Material afforded by further experimentation with the Szondi test confirms our original findings, which have been published in tabular form elsewhere. Thirty-one additional patients, making a total of 92 patients with multiple sclerosis studied, together with a breakdown of these patients into four groups, shows the same high incidence of the acceptance of dependency-needs in all groups. This is reflected in the Szondi test by the high "plus H" (acceptance of dependency) scores. A fifth group of patients, who had received treatment at the Kaiser-Kabat Institute, showed a lower percentage of such scores (table 12). We felt that this

TABLE 12 .- Percentage Within the Following Groups Who Showed Marked Plus H Scores

	Per Cent
Tabetic patients	. 90
Multiple sclerosis	
Advanced (hospitalized)	. 78
New arrivals at K. K. Institute	. 75
Advanced (home bound)	. 70
Mild	
Remission	. 69
Poliomyelitis	. 57
Families of multiple sclerosis patients	. 57
Patients at K. K. Institute after treatment	. 53
100 unselected males	. 53
100 neurotic males	. 46
33 nurses	. 42
20 theological students	. 35
100 female neurotic patients	
21 women medical students	. 21
261 women college students	. 15

decrease was at least indicative of the influence of the environment on this overdependent attitude.

The two extremes in table 12 are afforded by the women college students, at the one end, whose intellectual and "career" interests tend to minimize the dependency scores, and, at the other, the tabetic patients, who might be described as completely abandoned to the dependency position of their hospitalized status. Again, all multiple sclerosis groups, with the exception of those patients who have been receiving treatment at the Kaiser-Kabat Institute, have emphasized dependency scores.

Figure Drawings.—It is not possible to tabulate material from the Figure Drawing test in the same way as from the Rorschach, Szondi or Bellevue-Wechsler tests. In the first place, some of the patients were so handicapped as to be unable to complete this test satisfactorily. In the second place, there are no accepted norms. An atomistic breakdown of the material is not the most helpful way of presenting it.

We have contrasted one of the drawings of our multiple sclerosis patients with drawings obtained, and considered somewhat typical, of other patient groups. While we can say with certainty that not all patients in this group could be said to

produce similar figures, at the same time this type of drawing did not occur elsewhere.

Ouoting Modell and Potter,9 we may say:

In speaking of characteristic personality traits or conflict situations [in their case with hypertensive, ulcer, and asthmatic patients] we do not imply that these are specific characteristics found only in the disorder in question. As all of these are common psychopathological manifestations . . . we only imply that they are found with significant frequency and occupy a position of relative prominence in the character structure of the patients studied.

The Most Unpleasant Concept Test.—As was mentioned before, a full description of this test can be found elsewhere. The procedure is such that the patient is asked to think of the most unpleasant thing that comes to mind and, having thought of it, to draw it. Unfortunately, in our initial experiments we were struck by the difficulty that multiple sclerosis patients had in handling pencils and attempting to draw. Hoping to keep our findings uniform, we dismissed this test as impractical. However, we later developed a modification whereby the patient described his most



Fig. 1.—Outstanding as the characteristic of our largest control group, i. e., patients with neurotic disturbances, was the tendency to portray the human being in terms of the head alone. Despite the fact that the instructions were to draw a person, the neurotic subject in a large number of cases conceived of the person in terms only of the intellect and, for various reasons, chose to by-pass and ignore the body as a whole.

umpleasant experiences verbally. We have, therefore, findings on 112 of the 144 patients.

Our findings may be summarized briefly as follows: Among "normal" subjects, who were free from symptoms, the most frequent or "popular" responses to this test were as follows: The most unpleasant concept was damage brought about by the atomic bomb, i.e., the greatest disturbance to the greatest number that can be envisaged by the person. The second was a specific and concrete experience by which the individual had been traumatized; he remembered an actual unpleasant happening. As the third was listed death or illness, usually of a close relative.

Modell, A. H., and Potter, H. W.: Human Figure Drawing of Patients with Arterial Hypertension, Peptic Ulcer, and Bronchial Asthma, Psychosom. Med. 11:282-292 (Sept.-Oct.) 1949.



Fig. 2.—Drawing done by a patient with multiple sclerosis, indicating complete functional helplessness.



Fig. 3.—A less extreme, but typical, example of the multiple sclerosis patient's concept of a person. The multiple sclerosis patients tended to draw persons without hands, or feet, and in many instances with only partially completed legs. The man in our example appears to be walking on stumps. Even those persons with artistic ability portrayed their bodily handicaps by stiffness or obvious disproportions of the feet and hands or arms.

Our most striking findings in regard to this test related to the neurotic patients and those with a borderline psychosis. As is illustrated in figure 4, the neurotic subjects portrayed as the most unpleasant thing they could think of some small animal, such as a snake, insect, fly, rat or mouse.

Patients with a borderline psychosis portrayed a psychological experience or intense feeling as if it were objectified or in itself an entity.

It might have been expected that multiple sclerosis patients would consider their illness as the most unpleasant thing. Surprisingly, only 19 of 112 patients pictured this. The greatest number, 33 patients, portrayed or expressed the idea of the death of a close relative. In no case was the neurotic type of small animal or the

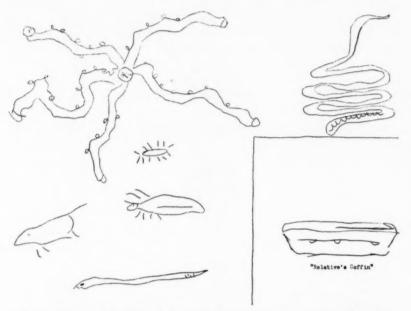


Fig. 4.—Drawings of neurotic patients in the Most Unpleasant Concept test. The majority of multiple sclerosis patients expressed the idea of the death of a relative (lower right).

psychotic portrayal of a state of feeling as an entity found. Only three of our 112 patients achieved the type of objectivity in regard to the question as a whole which results in the portrayal of the atomic bomb. It is surprising also to notice that 20 patients could think of nothing that was unpleasant in their lives or they resorted to some extremely trivial occurrence, such as once having failed in algebra in high school some 20 years ago.

It is also of interest that in no instance among the hospitalized patients, who were the most extremely incapacitated, was the selection of multiple sclerosis as the most unpleasant concept given. Where this response occurred, the highest percentages lay with the mild cases. Such a finding would suggest that the adjustment between health and partial disability seems to be an unusually distressing one.

This is reminiscent of Goldstein's finding in brain-injured patients, in whom minor visual defects caused acute distress, whereas gross lesions were accepted with almost blithe disregard.10

CONCLUSIONS

Although the bulk of the experimental findings have been presented in this paper, we expect to develop several facets of this study further. We shall include consideration of the findings with a view to differential diagnosis, particularly of multiple sclerosis and hysteria. We also wish to develop ideas arising from the meaning for the patient of these various test procedures and the possible psychotherapeutic value of the testing interview.

Pulling together our results thus far, we may say that a breakdown of the findings on the total number of patients, patients with remissions, patients with mild disease, patients with advanced disease and patients undergoing treatment at

the Kaiser-Kabat Institute has proved helpful.

Characteristic of the patients in remission has been a higher percentage of persons with superior intelligence, the lowest rate of persons showing scatter or erraticness of performance on the intelligence test. On the Rorschach test we find the highest group with the ambiequal personality type, showing the capacity for richer psychological experience and living. They have also the highest percentage of expanded personality types, which include the ambiequal, the introverted and the extroverted. A further characteristic of the remission group may be described as a more realistic willingness to allow the anxiety concomitant with physical symptoms to register as such in consciousness.

Characteristic of the patients with mild, early disease is also a moderate percentage showing extreme scatter on the Bellevue-Wechsler test. A pronounced swing toward constriction of personality type is reflected in the Rorschach findings. The greatest amount of overt distress is shown in the Most Unpleasant Concept test, in which the highest percentage related this experience to the illness itself.

Characteristic of the Kaiser-Kabat Institute patients are the lowest dependency scores, dropping from 75 per cent, as found in the new arrivals, to 53 per cent after treatment. These patients also show the greatest degree of extroversion on the Rorschach test.

It would appear that patients with advanced disease, whether home bound or hospitalized, show some effect of the disease on intelligence, in that they show both the lowest number of persons having superior or very superior intelligence quotients and the highest rate of erratic performance or scatter. They also show the highest number of the most extreme types of personality constriction. They have the highest dependency scores, and show a disregard of bodily symptoms, as reflected in the Rorschach test, to the most extreme degree.

Such changes within the group as the disease progresses, together with the modifiability of some of the traits by deliberate environmental effort, make it seem unlikely that the psychological characteristics could be considered as predisposing the person to the disease. It appears to us at this stage that our second hypothesis is the more tenable one. Such a disease as the multiple sclerosis process imposes certain standard conditions on the individual patient, leaving its mark to a greater or less degree, depending on the patient's premorbid personality structure.

^{10.} Goldstein, K.: The Organism: A Holistic Approach to Biology Derived from Pathological Data in Man, New York, American Book Company, 1939.

LASEGUE SIGN AND KERNIG SIGN

Historical Notes

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"You will find it very good practice always to verify your references, sir!" —Martin Joseph Routh (1755-1854).

LASÈGUE SIGN

HE STRAIGHT-leg-raising sign of Lasègue in sciatica (pain on raising the leg extended at the knee) is one of the best known in neurology. It ranks with those of Babinski and Romberg. Certainly there is no textbook on neurology or neurologic examination that fails to describe this sign. The present interest in the intervertebral disk has brought about a revival of the use of this time-honored sign, How, when and where did Lasègue first describe his famous sign? Ernest Charles Lasègue, of Paris (1816-1883), was an epidemiologist, internist, neurologist, and psychiatrist. In Volume 2 (1864) of the Archives générales de médecine, of which he was editor, he wrote an article,1 "Considérations sur la sciatique." This has become a classic. Naturally, it has been assumed by everyone that the sign was described therein. Indeed, when we consult leading textbooks on neurology (Oppenheim²; Wilson³), a handbook on neurology (Cohn⁴; Wertheim Salomonson 5), a medical encyclopedia (Kelly 6) and a monograph on sciatica (Lewin 7), invariably we find that Lasègue's article of 1864 is referred to when the sign is mentioned. In his article in Lewandowsky's "Handbuch der Neurologie," Wertheim Salomonson, referring to Lasègue's article of 1864, explicitly states: "Lasègue described. . . ." However, a thorough study of Lasègue's original article fails to disclose any description of the sign, or even any reference to it. Nor do any other earlier or later writings of Lasègue mention the sign. The fact of the matter is that Lasègue, who died in 1883, never described his sign. It is true that it was Lasègue who discovered the sign. In the wards of l'Hôpital de la Pitié he constantly examined for it, emphasizing its diagnostic significance to his pupils and stressing the fact that it is constantly present in sciatica.

The first description of Lasègue's sign was given, not by Lasègue, but in 1881 in Paris, in a doctor's thesis by Forst, a pupil of Lasègue. The thesis, presented on

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Lasègue, C. E.: Considérations sur la sciatique, Arch. gén. de méd. 2:558-580, 1864.
 Oppenheim, H.: Lehrbuch der Nervenkrankheiten, Ed. 7, Berlin, S. Karger, 1923, Vol. 1, p. 897.

^{3.} Wilson, S. A. K.: Neurology, London, Arnold & Co., 1940, p. 353.

Cohn, T.: Mechanotherapie, in Lewandowsky, M.: Handbuch der Neurologie, Berlin, Julius Springer, 1910, Vol. 1, Pt. 1, p. 1322.

^{5.} Wertheim Salomonson, J. K. A.: Neuralgie und Myalgie, in Lewandowsky, M.: Handbuch der Neurologie, Berlin, Julius Springer, 1911, Vol. 2, p. 1.

Kelly, E. C.: Encyclopedia of Medical Sources, Baltimore, Williams & Wilkins Company, 1948, p. 246.

Lewin, P.: Backache and Sciatic Neuritis, Philadelphia, Lea & Febiger, 1943, p. 699.
 Forst, J. J.: Contribution a l'étude clinique de la sciatique, Thèse de Paris, No. 33, 1881.

Jan. 29, 1881, by its 31 year old author, was dedicated to Lasègue, its sponsor, in France called président de thèse.

Forst mentioned that it was his teacher Lasègue who had first drawn his attention to the sign, but that nowhere until the time that he wrote his thesis had he been able to find in the literature a description of the sign. Forst considered it pathognomonic for sciatica and dealt only with its clinical and differential-diagnostic aspects. Forst explained the pain evoked by testing for the Lasègue sign as being due to pressure of the muscles on the trunk of the sciatic nerve. It was de Beurmann be who, in a much-cited article in 1884, gave the correct explanation for the Lasègue sign as being due to the stretching of the sciatic nerve. De Beurmann said:

Lasègue always looked for this sign and never failed to emphasize its value. We believe it was he who discovered it first, though he did not mention it in his article published in the *Archives de médecine* in 1864. It was described in 1881 in a doctor's thesis of one of his pupils, Forst.

Those who give as the source of Lasègue's sign his article of 1864 often simultaneously quote also the article of de Beurmann, as, for instance, do Wilson and Oppenheim. This means that the articles of Lasègue and of de Beurmann, though cited, have not been read carefully. The article of Lasègue does not contain any description of his sign of sciatica, and in the article of de Beurmann this fact is explicitly pointed out. What may well have happened is this: Someone, most probably Oppenheim, made the initial error of giving the source of the sign as Lasègue's article of 1864, and his statement has been uncritically repeated ever since. The French, however, correctly reported the historical fact (Pitres and Vaillard ¹⁰; Lévy-Valensi ¹¹); it is occasionally mentioned in other than the French literature (Hall, ¹¹⁸ Sjöqvist ¹²).

KERNIG SIGN

This sign (involuntary flexion of the knee on passive lifting of the leg, extended at the knee) ranks in popularity with that of Babinski, Romberg, and Lasègue. When did Kernig describe this sign? In 1884, say Garrison, ¹³ Garrison and Morton, ¹⁴ Wechsler, ¹⁵ Skinner, ¹⁶ Ziehen, ¹⁷ and R. W. B. ¹⁸ Ziehen gives 1884 as the year

^{9.} de Beurmann: Note sur un signe peu connu de la sciatique: Recherches expérimentales, Arch. physiol. norm. et path. 16:375, 1884.

^{10.} Pitres and Vaillard: Maladies des nerfs périphériques, in Gilbert, A., and Carnot, P.: Nouveau traité de médecine et du thérapeutique, Paris, J. B. Baillière et fils, 1924, Vol. 36,

^{11.} Lévy-Valensi, J.: Précis de diagnostique neurologique, Paris, J. B. Baillière et fils, 1925, p. 506.

¹¹a. Hall, G. W.: Neurologic Signs and Their Discoverers, J. A. M. A. 95:703-707 (Sept. 6) 1930.

Sjöqvist, O.: The Mechanism of Origin of Lasègue's Sign, Acta psychiat. et neurol.
 46:290-297, 1947.

Garrison, F. H.: An Introduction to the History of Medicine, Ed. 2, Philadelphia,
 W. B. Saunders Company, 1914, p. 570.

^{14.} Garrison, F. H., and Morton, L. T.: A Medical Bibliography, London, Grafton & Co., 1943, p. 256.

^{15.} Wechsler, I. S.: A Textbook of Clinical Neurology, Ed. 6, Philadelphia, W. B. Saunders Company, 1947, p. 776.

^{16.} Skinner, H. A.: The Origin of Medical Terms, Baltimore, Williams & Wilkins Company, 1949, p. 202.

in which the first communication on this sign appeared. Skinner,¹⁶ in his work of 1949 on medical terms, says: "First described by Kernig in 1884 it was not reported until 1907." Finkelnburg,¹⁹ Wilson,²⁰ and Fulton ²¹ give the date as 1907. The first group of authors referred to an article of Kernig's of 1884 which appeared in Russian ²² and in German.²³ The second group referred to an article by Kernig ²⁴ which appeared in 1907. However, Kernig described his sign even earlier than 1884. This was done, as mentioned by Hassin,²⁴ⁿ at a meeting of the General Society of St. Petersburg Physicians in St. Petersburg, on Sept. 21, 1882. The proceedings of this meeting appeared in German.²⁵ Kernig himself spoke on a "disease symptom of acute meningitis" which can be of importance for the diagnosis. This diagnosis of meningitis is difficult in the first stage of the disease.

[The symptom] consists in a sudden occurring tonic contraction of the musculature of the lower extremities affecting especially the flexors and is evoked in this way that one raises the patients or generally brings them to a sitting position. Due to this raising the legs assume a semiflexed position, and retain this position until the patients have been brought into their usual position in bed; only then the flexor cramp loosens without leaving any traces. The experiment can be repeated as often as one pleases. This phenomenon is often associated with simultaneous opisthotonic cramps of the neck and of the dorsal muscles.

In his works of 1882 and 1884, Kernig ²⁶ spoke of the elicitation of his sign essentially by having the patient lifted from the supine position in bed or, in particular, by having him sit up on the edge of the bed with the legs dangling. Only on the sitting patient did he try to stretch the leg at the knee. He always stressed the appearance of contraction at the knees merely by bringing the patient to a sitting position. In his article of 1907 only ²⁴ did Kernig describe the technique as it is now used.

One leaves the patient in the supine position and lifts the extended leg. It is held at the lower leg at the heel and an attempt is made to bring it extended to a right angle with the trunk. When this right angle is approached the contraction sets in.

This technique was introduced by William Osler,²⁷ whose article of 1899 contains an illustration of "Kernig's sign, showing the strong contraction of the flexors on attempting to extend the leg."

17. Ziehen, T., in Bruns, L.; Cramer, A., and Ziehen, T.: Handbuch der Nerevenkrankheiten im Kindesalter, Berlin, S. Karger, 1912, p. 929.

18. R. W. B.: Kernig's Sign, editorial, New England J. Med. 225:516, 1941.

 Finkelnburg, R.: Die Erkrankungen der Meningen, in Lewandowsky, M.: Handbuch der Neurologie, Berlin, Julius Springer, 1911, vol. 2, p. 1078.

20. Wilson,3 p. 14.

- 21. Fulton, J. F.: Physiology of the Nervous System, Ed. 3, New York, Oxford University Press, 1949, p. 112.
- Kernig, W. M.: On a Little-Known Sign of Inflammation of the Leptomeninx of the Brain, Vrach. 5:427-428; 446-447, 1884.
- Kernig, W.: Über ein wenig bemerktes Meningitis-Symptom, Berl. klin. Wchnschr. 21:829-832, 1884.
- Kernig, W.: Über die Beugekontraktur im Kniegelenk bei Meningitis, Ztschr. klin. Med. 64:19, 1907.
- 24a. Hassin, G. B.: Kernig's Sign and Its Pathogenesis, M. Rec. 68:413-415 (Sept. 9) 1905.
 25. Kernig, W.: Ein Krankheitsymptom der acuten Meningitis, St. Petersburg med.
 Wchnschr. 7:398, 1882.

26. Kernig, footnotes 22, 23 and 25.

 Osler, W.: The Aetiology and Diagnosis of Cerebrospinal Fever, Brit. M. J. 1:1517-1528, 1899.

INTRAMEDULLARY MALIGNANT TERATOMA OF THE SPINAL CORD

Report of a Case

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INTRAMEDULLARY teratomas of the spinal cord are rare. In a recent review of the literature, Sachs and Horrax 1 were able to gather only 25 cases of intraspinal teratoid and teratoma. This justifies the report of a case of a malignant trigerminal intramedullary tumor with clinical and pathological features which, so far as we have been able to ascertain, have not previously been reported.

REPORT OF CASE

Clinical Report.—J. L., a white girl aged 11 years, was first admitted to University Hospital in November, 1948, because of progressive weakness of the legs without pain. Three weeks previously she had onset of "weakness of the knees" and a shuffling gait and began to fall frequently. One week before her admission her left leg became numb, and a few days later she was no longer able to walk. She had no bladder disturbance.

Neurological examination revealed that the left leg was very weak and that the patient was unable to lift it from the bed when in the supine position, but was able to dorsiflex the foot weakly. The right leg was slightly stronger but was definitely paretic. The patient was not able to stand without support. The deep reflexes were increased, and there were a sustained ankle clonus and a bilateral Babinski sign.

Sensation to pinprick was reduced below the seventh thoracic dermatome on the right and somewhat diminished below the eighth thoracic dermatome on the left, but in the sacral segments sensation was intact bilaterally. Tactile and thermal sensations were decreased bilaterally below the eighth thoracic dermatome, thermal sensibility being more impaired on the right. The sense of motion, position, and vibration were impaired in both lower extremities.

There was no dermal sinus or spina bifida.

Roentgenologic examination (Munson Hospital, Traverse City, Mich.) showed that from the fifth to the ninth thoracic segments the vertebral canal was enlarged in both the anteroposterior and the lateral diameter to approximately twice the normal width (Fig. 1). Roentgenographic examination of the chest at this time showed nothing remarkable.

The spinal fluid was under an initial pressure of 150 mm. of water. There were no fluctuations and no rise of pressure on compression of the jugular vein. There were 10 cells per cubic millimeter, and the total protein was 1,860 mg. per 100 cc. Routine studies of the blood and urine revealed nothing significant.

A laminectomy was performed on Nov. 6, 1948 (Dr. Edgar A. Kahn). The sixth through the tenth thoracic laminas, which were distinctly widened and thinned, were removed, and a fusiform enlargement of the dura was exposed. The latter was opened, revealing a bifid spinal

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Sachs, E., and Horrax, G.: A Cervical and a Lumbar Pilonidal Sinus Communicating with Intraspinal Dermoids, J. Neurosurg. 6:97-112 (March) 1949.

cord continuous with a grayish neoplasm, which measured 5.5 by 3 by 2.5 cm. A longitudinal wedge-shaped resection of the main part of the tumor was carried out, together with decompression both upward and downward to the normal cord. The dura was left open, and the defect was covered with gelfoam. There was considerable pessimism regarding the return of any function, for it was thought that irreparable damage had been done to the cord.

After operation the patient improved rapidly, and two weeks later she was able to walk unassisted, although sensory examination showed little change from the preoperative status. She returned home and to school, and two and one-half months after operation a letter was received from her parents asking if it was permissible for her to play basketball and to be a cheer leader for her school. However, only two weeks later she again noticed dragging of the left leg, which became rapidly weaker. She was readmitted to University Hospital three and one-half months after operation.

Examination revealed that both legs were paretic. The patient could not raise the left foot from the table but could pull up the right leg. She was unable to walk but was able to sit up; tone and contraction of the abdominal muscles were good. Thermal sensation was grossly decreased from the fourth thoracic dermatome downward, being more affected on the right. Sensa-



Fig. 1.—Roentgenograms of the spine, showing an expanding lesion in the midthoracic region.

tion of superficial and deep pain was reduced bilaterally from the seventh thoracic dermatome downward, with greater impairment on the right. The sensations of vibration, motion, and position were diminished in both legs. The reflexes in the lower extremities were hyperactive, and there was an abortive ankle clonus bilaterally. The Babinski sign was elicited on both sides.

A decompressive laminectomy was performed on Feb. 22, 1949. A large tumor was seen to have recurred, involving the cord from the sixth to the tenth thoracic segment. Because of its size no attempt was made to remove it. X-ray therapy was carried out postoperatively. From March 1 to 15, 1949, a total of 2,475 r was administered in divided doses of 150 to 200 r over a 13 by 10 cm. field in the thoracic region (200 Kv. peak, 25 ma., 50 cm. target skin distance, 0.5 mm. Cu and 1.0 mm. A1 filtration, 1.0 mm. Cu half-value layer). Ten days later the patient was able to walk without assistance.

The patient led a normal life for nine months. She walked, ran, and rode her bicycle without difficulty, in spite of a slight residual weakness of the left lower extremity and partial bilateral loss of sensation below the seventh thoracic dermatome. Ten months after her second operation she had onset of headache and diplopia and began to vomit.

Neurological examination revealed minimal paresis of the right lateral rectus muscle. There was no papilledema, and except for the sixth, the cranial nerves were normal. Sensory

examination revealed bilateral hypalgesia and loss of two-point tactile discrimination and of perception of skin writing below the seventh thoracic segment, complete loss of sensation of vibration in the left lower extremity, and considerable reduction in the right. The sense of motion and position was absent in the left foot and was reduced in the right. The gait was ataxic and paretic, with a tendency to lift the feet too high. There was considerable lordosis of the spine. Strength was good in both upper extremities, poor in the trunk (as in rising from a lying-down position) and fair in the legs and feet; the only pronounced weakness in the legs was in the flexion of the left calf on the thigh and the thigh on the trunk. The knee and ankle jerks were pathologically hyperactive, with an abortive ankle clonus bilaterally. The Babinski sign was present bilaterally. Romberg's sign was elicited, with a tendency to fall backward. There were some dysdiadokokinesia and hypotonia in both upper extremities. Within a few days after her admission, papilledema was seen to develop bilaterally.

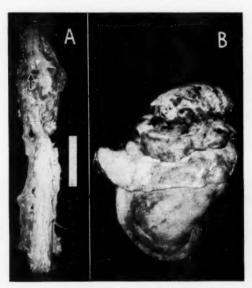


Fig. 2.—A, photograph of the spinal cord, showing bifurcation of the cord (arrow pointing to the left segment) at the upper pole of the intramedullary teratoma, thickened leptomeninges and small tumor nodules over the remainder of the cord. B, photograph of the lesion in the pleura over the anterolateral surface of the upper lobe of the left lung.

Roentgenographic examination showed that the skull was normal. The neural canal was of the same appearance as before, but examination of the chest revealed a large mass in the left anterior midthoracic region, which previously was not present.

The pressure of the spinal fluid was 400 mm. of water, and the protein content was 67 mg. per 100 cc.

A localizing electroencephalogram suggested a lesion in the posterior fossa, extending approximately from the midline to the right.

To relieve the symptoms, a right-lateral ventriculostomy was done, with some relief. Air studies showed enlarged ventricles without distortion or shift.

A suboccipital craniotomy on Jan. 28, 1950, revealed a tumor the size of a small green pea at the obex of the fourth ventricle. Dye instilled into the lateral ventricle through the previously placed trephine opening appeared almost immediately in the fourth ventricle, indicating that no block was present in the ventricular system; however, it was suspected that the communi-

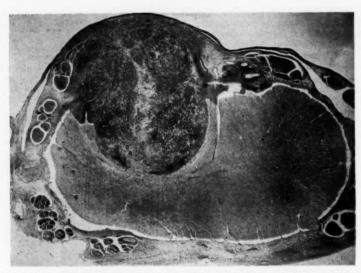


Fig. 3.—Photomicrograph of a cross section of the spinal cord, showing heavy infiltrations of tumor in the leptomeninges, compressing and destroying the adjacent cord. Hematoxylin and eosin; \times 8.

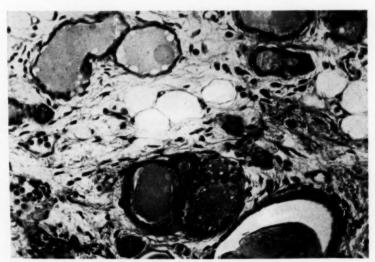


Fig. 4.—Photomicrograph of an area of the intramedullary teratoma, showing tissue of thyroid type (first operation). Hematoxylin and eosin; \times 200.

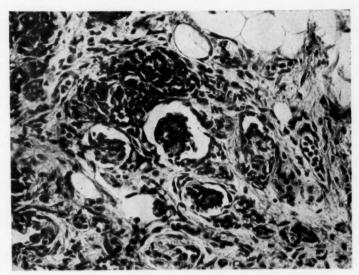


Fig. 5.—Photomicrograph of an area of the teratoma, showing imperfect glomeruli (first operation). Hematoxylin and eosin; \times 200.

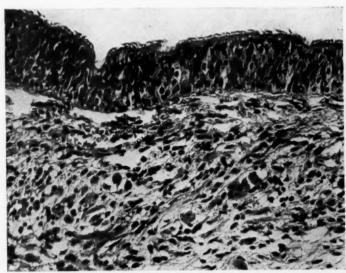


Fig. 6.—Photomicrograph of the lesion removed from the obex of the fourth ventricle, showing a cyst lined with ciliated columnar epithelium, with blastomatous muscle and spindle cells in its walls. Hematoxylin and eosin; \times 200.



Fig. 7.—Photomicrograph of blastomatous muscle cells in the leptomeninges of the spinal cord. Hematoxylin and eosin; \times 600.

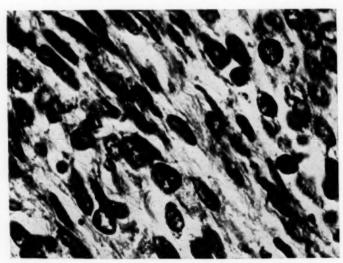


Fig. 8.—Photomicrograph of the spindle cells from the lesion in the pleura. Hematoxylin and eosin; \times 600.

cation channels, or foramens of Luschka, in the posterior fossa were blocked by tumor and that an obstruction would occur in a short time. Accordingly, a third ventriculostomy was performed. There was no improvement, and the patient died three and one-half weeks later.

Pathologic Examination.—Autopsy and Biopsy Material: The brain weighed 1,420 gm. There were marked edema and moderate clouding of the meninges over the pons and medulla. The lateral ventricles and the third ventricle were moderately dilated. The surgical ventriculostomy opening in the lamina terminalis was 4 mm. in diameter, and there was a free flow of cerebrospinal fluid at the time of autopsy. The fourth ventricle was greatly dilated but contained no visible tumor.

The spinal canal was dilated to twice its diameter laterally and posteriorly in the region of the fifth to the ninth thoracic vertebrae. In this area the dura was thickened and firmly adherent to the surrounding tissue. The segment of the cord removed was 23 cm. long; its wider portion was that of the thoracic segments, which measured 6 by 3.2 by 1.8 cm. In the latter area there was a soft, nodular tumor, white and covered with dilated, thin-walled vessels. At the upper pole of the tumor the spinal cord was bifurcated, and the right segment was slightly larger than the left. As these segments were traced downward, they became completely surrounded by tumor and were grossly indistinguishable from it. On the anterior surface of the spinal cord, above and below the main tumor, were several small separate nodules, which were oval and white. Two of these neoplasms involved roots of the cauda equina (Fig. 2 A). The leptomeninges were thickened throughout, especially in the region of the cauda equina.

Microscopic examination of the tissue removed at the first operation from the enlarged thoracic segment revealed a complex teratoma, composed of cartilage, bone, fat, mesenchymal tissue, smooth and striated muscle, imperfect glomeruli, thyroid, blood vessels, primitive glands lined with columnar epithelium, nerve tissue and focal accumulations of cells with irregular, dark nuclei and scant cytoplasm, some of which appeared spindle-shaped. In this region mitotic figures were seen. The tissue removed at the second operation showed a similar structure (Figs. 4 and 5).

The leptomeninges of the spinal cord presented an unusual histologic picture in that they were heavily infiltrated with tumor cells of striated muscle. These cells contained a centrally placed nucleus and thin elongated cytoplasm, occasionally branched. In the more mature cells both longitudinal and crossed striations were distinct, while in others the striations were rudimentary; some resembled smooth muscle cells (Fig. 7).

The small tumors above and below the enlargement of the cord were composed of dense masses of blastomatous muscle cells, which compressed and destroyed the adjacent cord substance and infiltrated its perivascular spaces (Fig. 3). Myelin preparations showed demyelination in the posterior and lateral columns. The tumor tissue between the two segments of the thoracic portion of the cord was that of the complex teratoma.

The tumor removed from the obex of the fourth ventricle was of different structure; it was a cyst lined with ciliated pseudostratified columnar epithelium, placed on a wide layer of striated muscle and spindle-shaped cells (Fig. 6).

The leptomeninges of the medulla and cerebellum and the floor of the fourth ventricle were invaded by blastomatous muscle cells.

In the left pleural cavity there was a soft, circumscribed, oval tumor which measured 11 by 9 by 4.5 cm. and was firmly attached to the anterolateral surface of the upper lobe of the lung (Fig. 2B). Caudal to this tumor there was a smaller neoplasm, measuring 2.5 by 1.2 by 0.6 cm., on the parietal pleura. Section of the tumor revealed areas of soft gray-white and firmer yellow-brown tissue and numerous small cystic cavities.

The tumor in the chest was built of spindle-shaped cells with poorly visible striations, apparently blastomatous muscle elements; they were mostly arranged in bands surrounded by a delicate connective tissue network (Fig. 8). Occasionally they formed a primitive glandular pattern. In many areas no definite pattern could be seen.

The histologic diagnosis was that of a malignant trigeminal teratoma with extensive invasion of an adenorhabdomyoma into the pleura and throughout the spinal cord and brain stem.

COMMENT

As has already been mentioned, this case belongs to the comparatively rare variety of trigeminal teratomas of the spinal cord. Of the 25 cases collected by Sachs and Horrax, only 10 were of true intraspinal teratomas. Most of these tumors were attached to or connected with the cord, but none actually replaced and infiltrated the tissue of the cord, as in our case, nor were metastases reported.

According to Ingraham and Bailey,² these neoplasms are relatively benign, and even incomplete removal frequently relieved symptoms for a long time. One of their patients (originally reported by Kubie and Fulton³) was well 19 yr. after partial removal of the tumor. Our patient similarly showed a gratifying relief of symptoms after partial removal, decompression and X-ray therapy; but the essential malignancy of the tumor asserted itself, and death occurred 15 mo. after the first operation.

The terminal symptoms of increased intracranial pressure in our case presented an additional diagnostic problem and were interpreted as being due to an obstructing lesion, possibly in the fourth ventricle, whereas in reality they were caused by an obstruction of the subarachnoid channels of the posterior fossa.

It is reasonable to assume that the intramedullary tumor was the source of the implantations along the leptomeninges and in the pleura. These implants displayed two cell types: The undifferentiated cells in the leptomeninges gradually developed into the more mature rhabdomyoma cells. This explains the transitional cell types in various parts of the tumor, particularly in that of the chest; but here an additional feature was that of an abortive attempt at gland formation. The epithelial component of the implants was seen best in the lesion in the obex. It is probable that the latter represented an ascending implantation, rather than a second teratomatous lesion. The presence of the diplomyelia in this case suggests that the tumor had its origin early in the life of the patient.

SUMMARY

A case of malignant trigeminal teratoma of the thoracic portion of the spinal cord with extension to the meninges and pleura is described. In the early phases of the illness the neoplasm presented signs and symptoms of a tumor of the spinal cord, whereas in the terminal stages symptoms of increased intracranial pressure appeared as a result of obstruction of the subarachnoid communicating channels of the posterior fossa.

Ingraham, F. D., and Bailey, O. T.: Cystic Teratomas and Teratoid Tumors of the Central Nervous System in Infancy and Childhood, J. Neurosurg. 3:511-532 (Nov.) 1946.

Kubie, L. S., and Fulton, J. F.: A Clinical and Pathological Study of 2 Teratomatous Cysts of Spinal Cord, Containing Mucus and Ciliated Cells, Surg., Gynec. & Obst. 47:297-311 (Sept.) 1928.

Special Article

PSYCHIATRY WITHOUT FREUD

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FEEL sure that each of you, learning that my subject was to be "Psychiatry Without Freud," quite simply assumed that I was indulging in a pious fraud. Your assumptions, I must admit, speak well for your perspicacity, for it is a fact that I favored the title for two reasons. First, because it is provocative—and then because it is a "pious fraud." Psychiatry, that is, present day psychiatry, without Freud, and without all that has been added to it by his disciples and followers, is difficult to conceive. A recitation that literally considered psychiatry without Freud would be of interest only historically—and most likely would be a confounding, if not a "lugubrious," story. Yet lest you also assume that I purchased your interest by a trick, I must add that, though the manner was something of a fraud, the intent remains pious, and that once beyond this point, I am, and shall remain to the end, very much in earnest.

Let me plunge into the issue directly, but by means of a tale, of which it may be said, with the Italians, "Si non e vero, e ben trovato"—"If it isn't true, it is well found." The story goes that when the Eiffel tower was erected in Paris it came to the mind of one bright person to set up a powerful arc lamp right at its very topmost point. In this wise he thought to illuminate the entire surrounding park. He tried it; and it was indeed very beautiful. But it soon became apparent that, though it was truly brilliant, it did not work well. For those who came near were blinded by the light, and those who were at a distance were blinded by the dark. It had to be given up; and, as you know, the park about the tower has ever since been effectively illuminated by many lamps, none as bright as the original, but all of them placed at the dark spots all around.

If this tale is taken not too literally, and be transposed not too exactly, it does have its application to the "state of illumination" in psychiatry. Freud is its brilliant arc at the topmost point of the edifice—blinding when too near and obscure at the outskirts. Of course, the fault is not Freud's, and, like so much in human communication, the foregoing sentence is shot through with "scapegoat animism." "Galen retarded medicine for a thousand years," the historian writes. But it is hardly Galen's fault that for a thousand years none took courage to do by Galen as Galen did by others. It is, however, a fact that for too many, especially among the young psychiatrists, the brilliance of Freud is blinding, and blinding in many ways. They seem to labor in the belief that before Freud there was little or nothing worthy of the name psychiatry; that all antecedent psychiatric history was but the forerunner to a fulfilment achieved in Freud and in analysis. This is a sad delusion;

yet its practical consequences are minor, since the past has its historic realities which persist despite neglect or misunderstanding. Of greater consequence is what happens now and in the future. In this relation we see far too many among the Freudians "stomping the treadmill of orthodoxy," to prove what has been proved, many times over. Far too few venture to reassess the formulations, to test the assumptions and to challenge the procedures by which they function. Yet there is a science in the asking of questions no less intricate and valuable than the science of finding answers, and empirical effectiveness unless hedged on all sides by challenge and question is like a desert, where for the want of gage marks one is easily lost.

There is, as you know, no dearth of psychoanalytic literature, but most of it is devoted to confirming what has been affirmed time and time again. I for one should like to see, not another instance spelled out in years of analysis, where the sight of the primal scene at the age of 2 is held to account for the vaginismus at the age of

20, but, rather, something new, and critical, and very pertinent.

I should be interested, for example, in a reassessment of the Oedipal cycle. Is the version now current fully adequate? Does it embrace the whole of the mythological tale and of the psychiatric experience? I have come to feel—and this by clinical experience—that the incest motif is but half the tale, that the real tragedy is derived from the fault of Laius, the father of Oedipus, rather than from Oedipus proper. For it was Laius, as you will recall, who craved a son, and it was he who sought to evade the fate foretold by the oracle, should he have issue. Who knows how the fates might have softened had Laius not bound the pierced feet of the child Oedipus and had he held him dear instead of exposing him on Mount Citheron. I am inclined to see in the tale of Laius and of Oedipus the embodiment of that primal wisdom which in the Hebrew is tersely versed in the phrase "The sins of the father shall be visited upon his children even unto the third generation."

I am not eager to advance these thoughts on the Oedipal cycle as otherwise than probationary; yet I think it more proper and more profitable to ask such questions than to repeat, in the adulation of a master, "The little boy seeks to possess his mother; the little girl, to displace her mother at the father's side," true though this may be. It were likewise profitable to study intensively the question of questions the dynamics of the therapeutic result. How is the cure effected; when effected? Such study would involve a host of collateral inquiries. For example, how passive is passivity, and how free is free association? Much profit could be derived from the further, and critical, study of dreams. There appears to be not only a determinable meaning to the dream content, but meaning also in the pattern of the dream proper; there is, in other words, a morphology of dreams. Psychoanalysis has been called ego psychology; yet the ego per se has received but limited study in recent decades. Here, certainly, is a subject of nuclear importance. No less significant, since it is involved in so much of psychopathy, is the superego; yet there have been few studies devoted to its nature and derivation since Freud, first, and Jung, later, enunciated their respective theories and beliefs. All these matters are not essentially of an academic nature, worthy of pursuit in a leisure and fancy-free hour. The defense offered by one who was recently confronted by just these questions that "we are too busy doing things to be much concerned with how we do them" is in effect degrading. For these questions are vitally concerned with "the doing of things," and it is more than likely that in being concerned with how we do things we may be enabled to do them better. Considering the duration, the costliness and

the not ever certain issue of psychotherapy, it would seem that any inquiry as to how we might function better should be not only welcomed but deemed the better part of discretion.

It was not my intention to set up a protocol for research and study in psychoanalytic theory and practice. In raising the few questions presented above, I meant only to illustrate where, and how, some of our younger men might leave off "stomping the treadmill of orthodoxy" and venture to illuminate those dark spots remaining.

The advent of Freud was one of the great historic experiences, and those who have compared him to Copernicus and Darwin did not indulge in spurious analogies. Freud "shook the world." He did what but few men in human history have done, that is, redirect human thought; create a new alphabet, a new vernacular and a new literature which not merely is corrective of certain segments of our inherited culture and credence, but, more, has opened up vast and new spheres of experience and learning. Freud has made available to us a new body of knowledge and also the instrumentalities by which that knowledge can be further extended. I think of him as I would of Loewenhoek, who not only uncovered the world of the infinite, but also shaped the tools for its exploration.

It is easy to apply superlatives to the name of Freud. One can do so without the hazard of contradiction, either now or later. But it is not so easy to specify just wherein particularly lies Freud's superlative desert. This is a most interesting and involved question, and whatever answer comes easily to mind by that very token may be considered wrong. Merely to hint at the intricacy of this problem, it is a fact that the greatness of such as Copernicus, Darwin and Freud is historically perceived to derive not from what knowledge they added, but, rather, from the influence they exercised. There is a relationship between the two, of course, but not in any sense commensurate. The knowledge, as in the case of Darwin, may even be grossly at fault; yet the influence, the impact, on human thought and destiny is, and remains, both salutary and enduring. I do not intend to expand on this theme; vet since it will advance my thesis, I want to offer this additional observation, Obviously, Freud's fame rests on his creation of psychoanalysis. This affirmation embraces all that entered into the genesis of the science of analysis—the discovery of the unconscious; the mechanisms of repression, the disguised emergence of the repressed; the identity and reciprocal interrelationships of the id, the ego and the superego; the function and meaning of the dream, and of everyday mischance and mishap; the technique of free association, abreaction and all the rest. But all of this does not account for all of Freud's fame. Nor does it account, on the other hand, for the enormous and intensive antagonism which Freud evoked among his contemporaries, and still does today among some persons, and peoples. I do not presume to have the full or final answer to the sources of Freud's fame, or his defamation. For that, there would be need of a longer perspective than the present offers. But I would add to the accounts of his eminence one consideration too much neglected and too little understood. I should, however, confess that what I advance is one of my own and fond conceits, which, though propounded for some years, has not received the recognition it deserves. Freud shocked the world of science and of intellect in arguing and in demonstrating both the rationality of the irrational and the irrationality of the rational. The first of the two propositions was the less opposed; the second aroused frenzied resentment. It is this split with the formal rationalism of his age that distinguishes and separates Freud from his contemporaries in science and psychiatry.

I recently found an ally to my thesis in odd quarters, and I shall quote him briefly. Isaiah Berlin, fellow of New College and university lecturer in philosophy at Oxford, wrote a most interesting essay entitled "Political Ideas in the Twentieth Century." 1 Part of Berlin's thesis is that the twentieth century is sharply separated from the nineteenth by a barrier which "divides what is unmistakably past and done with from that which most characteristically belongs to our day."

. . . The familiarity of this barrier must not blind us to its relative novelty. One of the elements of the new outlook is the notion of unconscious and irrational influences which outweigh the forces of reason; another the notion that answers to problems exist not in rational solutions, but in the removal of the problems themselves by means other than thought and argument.²

It was the firm faith of the nineteenth century that "la raison a toujours raison, that memories and shadows were less important than the direct perception of the real world in the clear light of the day." ³ These were the common assumptions of the rationalistic enlightened world. It is true that these assumptions were challenged and denied by a few isolated, "eccentric" thinkers—Carlyle, Dostoievski, Baudelaire, Tolstoi, Nietzsche. However, none of these was "a man of science," and hence none of them really challenged science. Such discomfiture as they caused to science could be neutralized by anatomizing them and exposing, as Max Nordau did, their "degeneracy."

Berlin counts Freud among the isolated and eccentric thinkers, who, "by giving currency to exaggerated versions of the view that the true reasons for a man's beliefs were most often very different from what they themselves thought them to be, being frequently caused by events and processes of which they were neither aware nor in the least anxious to be aware . . . helped, however unwittingly, to discredit the rationalist foundations upon which their doctrines purported to rest." 4

Freud, unlike the other isolated and eccentric thinkers, was a man of science. Though many a Nordau tried it, Freud could not be anatomized or his "degeneracy" exhibited for the pleasure and profit of the intellectual pharisees. He stood forth an obdurate challenge to the naïve rationality of the nineteenth century, and he endures as such to this day.

The antirationalism of Freud proffers some deep and challenging problems—in epistemology, in the dynamics of therapy, in esthetics and morals—problems which few have braved, but with which we must soon come to grips. Fortunately, the "soon" is not now, and I am thus left free to further pursue my thesis.

The subject matter of psychiatry without Freud is Freud's psychiatric contemporaries. It is to them that we must now turn our attention. At the outset, it is worth noting again that these contemporaries of Freud, unlike him, were partisans of that rationalism which rested its faith on "the direct perception of the real world in the clear light of day." By bearing this in mind we shall be helped to understand

^{1.} Berlin, I.: Political Ideas in the Twentieth Century, Foreign Affairs, pp. 352-385, April 1950.

^{2.} Berlin,1 pp. 356-357.

^{3.} Berlin,1 p. 360.

^{4.} Berlin,1 p. 369.

much, both of their shortcomings and of their merit and worth to present day psychiatry.

The nineteenth century was much preoccupied with psychiatry. In this period lived and worked Caesare Lombroso, Jean Martin Charcot, Wilhelm Griesinger, Theodor Meynert, Richard von Krafft-Ebing, Moritz Romberg, Karl Wernicke and Emil Kraepelin, to name but a few of the most eminent. These men advanced enormously the nosography of psychiatry and contributed substantially to psychotherapy. They were engaged in passionate and long-enduring apposition of psychiatric theory and concept, some being somatocists and others functionalists. Their disputations are overshadowed by those waged today; yet one can with much profit return to them and perceive how keenly they dealt with the issues which, remaining unsolved, still trouble us. Prominent in their thinking and in their polemics is the issue of the so-called psychosomatic disorders. Seemingly, they had as fine a grasp of the matter as any current.

In relation to the nineteenth century Freud stands, at least professionally, in an anomalous position. He was born in 1856 and died in 1939. He bridged both centuries, "inherited" the psychiatry of the nineteenth century, but in effect initiated that of the twentieth; and, as I have noted above, the twentieth century is in essential respects discontinuous with the nineteenth century. Because of this, it is something of a puzzle to determine who properly should be counted as Freud's psychiatric contemporaries. Certainly, the calendar cannot be taken as the sole arbiter. I have breached this puzzle by selecting three persons, and I have chosen them not solely on the basis of the calendar, but also because of their professional and theoretical proximity—because they broach on Freud's thinking and work. I have selected them also because their respective works still have a vital bearing on psychoanalytic psychotherapy.

The three I shall consider are Pierre Janet, Pavlov and Adolf Meyer. Janet was born in 1859; Pavlov, in 1849, and Meyer, in 1866. Of the three, Janet comes closest to Freud, both in age and in his theoretical formulation of psychodynamics. With the latter this is so much the case that partisans, more passionate than informed, have charged both Janet and Freud with having "stolen" one from the other. There is, however, no evidence to support such charges of plagiarism; and, though there is great parallelism between Freud and Janet, they each ultimately arrive at conclusions unmistakenly and widely divergent.

Janet is in his own rights a remarkable figure. His erudition was vast; his accomplishments were enormous. He was well grounded in medicine, in general and in neuropathology and in psychology. He was qualified in philosophy; he was a botanist of note. He was an indefatigable collector of data and of records. He wrote copiously and lectured widely. Yet, oddly enough, Janet is oftener condemned for his sins of omission than he is praised for the virtue of his achievements. Worse than that; he is badly neglected, at least outside the Latin countries. Freud contributed to this. His polemic against Janet falls short, both in justice and in objectivity. In his "Autobiography," he gives an inadequate summation of Janet's views on hysteria and then dismisses Janet as one who "behaved ill, showed ignorance of the facts and used ugly arguments." ⁵

^{5.} Freud, S.: Autobiography, translated by J. Strachey, New York, W. W. Norton & Company, 1935, p. 57.

Janet is blamed for not "having been Freud," for not having discovered, despite his enormous labors, the theory of repression, which in psychoanalysis "is the foundation stone of our understanding of the neurosis." Janet rested his theory of the neurosis on the lack of an adequate psychic tension, on what he termed psychasthenia—on weakness of the psyche. There is, of course, no doubt that Janet not only failed to discover the theory of repression, but also that he never fully accepted it. In his "Psychological Healing," ⁶ Janet writes:

. . . This conception of repression is undoubtedly one of the most interesting in the Freudian psychology. My own opinion is that the phenomenon must be explained in a different way, but it is none-the-less of great importance.⁷

What troubles Janet is "why the Freudians have extended the conception in this way, which is, to say the least of it, strange?" On this score, Janet ventures the opinion:

. . . The reason is that they want at all costs to discover a traumatic memory underlying every neuropathic symptom, to disinter a more or less modified memory of an event which has stirred the subject's emotions. . . . Repression as we have described it, is not a normal phenomenon which, through clumsy handling, becomes the cause of subsequent disturbances; it is itself already a morbid disturbance.⁸

This opinion follows on one to the effect that "in normal life, repression leaves no traces." Here Janet touches on a provocative theme, for since repression is a normal function in normal life, why, then, does it engender neurotic behavior in some but not in others? The answer cannot entirely rest on the nature of the material repressed. Freud comes close to Janet in the judgment he advances:

. . . It may be assumed that neurosis hardly ever develops unless there are constitutional or congenital factors increasing the possibility for such a condition.9

Despite their protestations, and Janet pokes a rather mordant wit at Freud and at psychoanalysis, there is much reciprocally illuminating in the works of Freud and Janet. I can subscribe to Mayo's statement:

It is the fashion in these days to dismiss, somewhat cavalierly, the work of Janet as something that has been superseded by Freudian and other developments. . . . The outcome is unfortunate, for there is no real conflict between the observations of Janet and Freud. Indeed they work in different parts of the same field so that their researches are mutually complementary; and any one person trained in the findings of one only is probably committed to incomplete understanding.¹⁰

There is a fiction current that Janet is a therapeutic pessimist, that he regards the psychoneurotic patient as a stigmatized degenerate for whom and with whom little can be done. Wittels 11 writes:

. . . Before Freud appeared on the stage the scientific explanation of neurosis was that it was all due to heredity and degeneration. The influence of heredity is undeniable, but the admission of this fact does not help us to cure our patient.

^{6.} Janet, P.: Psychological Healing, translated by E. and C. Paul, London, G. Allen & Unwin, 1925.

^{7.} Janet, p. 610.

^{8.} Janet, 6 p. 646.

Freud, S.: The Problems of Lay-Analyses, translated by A. P. Maerkers Branden, New York, Brentano's, 1927, p. 169.

^{10.} Mayo, E.: Some Notes on the Psychology of Pierre Janet, Cambridge, Mass., Harvard University Press, 1948.

Wittels, F.: Sigmund Freud: His Personality, His Teaching and His School, translated by E. and C. Paul, New York, Dodd, Mead and Company, 1924, p. 122.

Actually, however, Janet is anything but a therapeutic pessimist, and his thesis concerned with psychological tension and psychasthenia is grossly misunderstood and misrepresented by many analytically oriented writers. Janet is pessimistic with regard to psychotherapy as a science. "Psychotherapy does not yet exist. . . . We are merely beginning to see what it ought to be and what in due time it will become.\(^{12}\) But it is otherwise with regard to the practical effectiveness of psychotherapy; on this score Janet affirms:

Psychotherapy in the wider sense of the term, including within its scope all the methods of treatment based upon a knowledge of psychological or physiological laws, has unquestionably done good service in a very large number of cases.¹³

However, no matter how badly Janet is misunderstood or misrepresented, the fact remains that there is a cardinal difference between the psychiatric orientation of Freud and that of Janet. To summate this difference in terms of repression and of psychasthenia is both correct and convenient. Dalbiez, 14 who has treated the contrasting theories of Freud and Janet sympathetically and exhaustively, represents the difference in the following terms:

Janet has emphasized only such sources of illness as arise from material causality, while Freud has studied only such as derive from efficient causality. . . . In metaphysical language, we may say that Janet's schema derives from the concept of privation; Freud's, from that of opposition.¹⁵

In thinking on this, one is prompted to ask whether this difference in schemata did not derive from the nature of the material with which they, Freud and Janet, respectively dealt. In a passage which no doubt roiled Freud, Janet quoted approvingly the theory advanced by Friedländer and Ladame to the effect that there must be a peculiar kind of sexual atmosphere in Vienna—a sort of local demon, which, by epidemic as it were, takes possession of the population, so that in this environment the observer is foredoomed to overestimate the importance of sexual influences. One need not agree that the Viennese "overestimated the importance of sexual influences" to appreciate that the cultural, and hence the psychological, atmosphere of Paris differed from that of Vienna at the turn of the century. It may very well be, therefore, that Janet saw many more cases of deprivation than of opposition, and Freud more of opposition or repression than of deprivation.

This matter is of more than historical interest to us, for it is a fact, reported on by many, that the types of cases widely seen today are not of the classic type first reported by Freud, but are more commonly mixed cases, in which deprivation plays an important etiological role. In the treatment of such patients it is necessary not only to uncover repressed material, but also to conserve, to reenforce, to redirect what Freud calls libido, ¹⁷ and Janet, psychological tension. This involves not merely

^{12.} Janet,6 vol. 2, p. 1206.

^{13.} Janet,6 vol. 2, p. 1212.

^{14.} Dalbiez, R.: La method psychanalytique et la doctrine Freudienne, Paris, Descleé de Brouwer & Cie, 1936.

^{15.} Dalbiez,14 vol. 1, p. 191.

^{16.} Dalbiez,14 vol. 1, p. 620.

^{17.} Libido—"the chief goal, purpose, pattern or wish of ... conduct or behavior is the continuance of life. . . . That aspect of the transformed energy that pursues this creative goal, either within the body structures, as seen in growth or repair, at biological levels, as seen in mating,

the reintegration of such libido as is invested in the repressed material, or in "complexes," but often the addition to, or the increment of, the total libido available to the patient. Ferenczi, one of Freud's most able disciples and co-workers, came to this very conclusion and affirmed it to be incumbent on the physician, the psychotherapist, to reenforce, even to add to, the patient's libido. Few have followed Ferenczi's lead, at least among those who work outside the hospitals. It should be noted in this connection that a great deal of what is done in some of our better hospitals, independent of specific psychotherapy, is aimed at reenforcing and increasing the patient's libido.

In the mixed case, wherein etiology involves both repression and deprivation, it is frequently a question of which of the etiological factors should be dealt with first, and often it is better, indeed at times imperative, that before the repressed material is uncovered, the psychological tension, the libido of the patient, should be fortified. I recall a patient, a woman of 25, who, having tuberculosis, also suffered from anorexia nervosa, globus hystericus, vomiting, confusion and apathy. That she was suffering from a series of hysterical manifestations was clearly evident. That her neurosis derived primarily from "repression" could not be doubted. The sexual content of her symptoms was patent. This young woman had married some three years before, to escape her home. Her sexual experience was most unsatisfactory; coitus was usually per anum. She took the initiative in annulling her marriage and was encouraged by her parents, themselves rather inadequate persons, to return home. A futile and hopeless "asexual romance" filled the next year. That coming to an end, the patient reverted to her divorced husband, resuming her correspondence with him. He was serving at a military outpost. Her tuberculosis was discovered at about this time. When I first saw her, she was seeing her ex-husband two or three times a week, in the home of her parents. She indulged in some sexual play but not in intercourse. She accepted money from her ex-husband but was not certain that she wanted to remarry him. When she first came under my care, this young woman, standing 5 feet 8 inches (173 cm.) in stockinged feet, weighed 98 pounds (44.5 Kg.). It was painfully clear to me that in this patient's care I should need first to deal with her deprivations, and only later with her repressed material.

I grant that the case cited is of an extreme nature; yet I am convinced that too little attention is generally given to the current libidinal dynamics of the patient, more thought and energy being devoted to the ferreting out of repressed, painful, distorted memories which, it is of course true, contribute to the genesis of the neurosis. Yet a strengthened ego, fortified by a rich libido, is better able to meet and to reintegrate repressed materials. I suspect that the task of dealing with the current libidinal dynamics of the patient requires closer study of the patient's needs and involves greater therapeutic initiative than some therapists are willing or able, to assume.

I would conclude my treatment of Janet by affirming that we cannot further neglect the thesis of objective energy, so ably formulated by him. Its incorporation in the conceptualization of the genesis of psychopathy not only will better illuminate the dynamics of disorder but should enable us to prove more effective, in terms of

or at socialized levels as operating for family formation, works of art, invention, civilization, and culture, has been called libido by Freud. Within the body it acts as a force, a tension, an impulse" (Psychoanalysis Today: Its Scope and Function, edited by A. S. Lorand, New York, Covici-Friede, Inc., 1933).

the economy of time and effort, in treatment. Certain it is that our experiences during the last war, both with the military and with the civilian populations, without in any way invalidating Freud's thesis on repression, has fully validated Janet's ideas on psychological tension and psychasthenia. It is revealing and pertinent that what was called shell shock in 1918 was in World War II renamed combat fatigue. Without yielding aught to the mechanists, we can yet accede that all living organisms, from the lowest of plants to the highest of men, are transformers of energy. How much and how well man absorbs, transmutes and expends his energies is in part the concern of the psychotherapist.

From Janet, I would now turn to the second of Freud's "elected contemporaries," Ivan Pavlov. His work on the conditioned reflex touches but a segment of
Freud's psychiatry; yet this contact is of great importance. Those who have a guardianship interest in psychiatry would do well to watch the resurgence of Pavlovianism, promoted in part by the authoritarian countries, but also by those whose
predilections are for the concrete, the palpable, the directly mensurable. We are
likely to dismiss Pavlovianism as a past movement which came to an inglorious end
in behaviorism, and the ghost of which came to life here lately in a treatment for
inebriety. Such a dismissal is unwarranted and hazardous. The simplicity of Pavlovianism has a fatal appeal, to which many of the unwary must succumb. The
great ado about shock therapy and psychosurgery and all the recently developed
physical and chemical modalities of treatment have given new life to Pavlovianism.
Thus, for example, Masserman 18 takes a fling at psychoanalysis, stating:

Even in relatively enlightened spheres of psychiatry there are relics of animistic thinking: tide the substitution of the Freudian terms of "Id," "Ego" and "Superego" for the gods that in ancient times were thought to be in control of man's passions and intellect; or the attempts by some psychoanalytic mythologists to use the Narcissus and Oedipus legends, not as poetic allegories but as proofs of the supposed nature of man's unconscious conflicts!

Masserman is persuaded that his poor, bewildered cats, subjected alike to artificial conditioning, under artificial conditions, and then to arbitrary insult, will yield him better insight into the psyche of man than will the "mythology" of the psychoanalysts! It is not, however, the new behaviorists that need concern us here, but, rather, the bearing which Pavlov's work has on Freud's theories. Pavlov significantly confirms Freud's theory of conflict as a source of neurotic disorders. The classic demonstration of this is to be seen in the instance of the dog conditioned to distinguish and to respond appropriately to the exhibition of a circle and of an ellipse. All goes well as long as the two figures, circle and ellipse, are fairly distinguishable. When, however, the difference is reduced so that the oval is close in shape to the circle—ratio of axes, 8:9—the dog is thrown into a neurotic state. He becomes nervous, whines on the stand, twists and turns, and snaps at the apparatus. Pavlov accounts for these reactions as follows: 19

. . . Broadly, we can regard these disturbances as due to a conflict between the process of excitation and inhibition which the cortex finds difficult to resolve.

Dalbiez writes:

Pavlov's method will do us the service of bringing the problem of the etiology of the neuroses down onto the terra firma of experiment. It affords irrefutable proof of the existence of neurotic disorders due to a clash of opposed forces,²⁰

^{18.} Masserman, J.: Experimental Neurosis, Scient. Am. 182:38 (March) 1950.

Dalbiez, however, does not, as Masserman does, naïvely equate the neuroses of the dog with the neurosis in man. Psychology cannot be reduced to physiology. "Pavlov only studies movements," Dalbiez writes, "whereas Freud analyses cognitive or affective states and movements, cognitively—affectively governed." ²¹ He quotes approvingly Leibnitz' dictum to the effect that reflexology is true in what it asserts, and false in what it denies. ²¹

These considerations lead us back to the conditioned reflex. This is a physiological mechanism which subserves vital objectives, chiefly in the orientation of the organism toward the outer world. The condiitoned reflex can acquire a psychological character when the stimulus which acts as the conditioner is of a psychological nature. Most pertinent to our deliberations, however, is the simple fact revealed by Paylov that it is possible to "condition behavior," that is, to associate a stimulus (among humans, also an affect) with a motor, or behavior, pattern, in a causal relation. By the variety of stimuli utilized by Pavlov in his laboratory, it is evident that outside the laboratory the linkage of stimulus to behavior pattern is fortuitous; any combination is theoretically possible. Of course, as far as human beings are concerned, this theoretical possibility is never realized "in full"; human beings are not naturally "in harness on the experimenter's table," nor is the field as clear-too many conditionings are likely to be experienced simultaneously. Yet, as clinical experience shows, a good deal of psychopathy has the character of a "conditioned reflex," in the sense that a stimulus situation evokes a behavior reaction that is practically automatic and repetitive. It is also unsuited, ineffective and at times overtly destructive. The genesis of such a behavior reaction does not invariably derive from repression or conflict. It may be, and oftenest is, derived from a fortuitously determined association of stimulus situation with a motor or affect coincident. It may be, in other words, and in effect, an instance of malinstruction, of mislearning, or rather of learning what was valid as a particular but is not valid as a universal. The son of a harsh, domineering, brutal father will most likely associate the "father person" with unpleasant affects and react in a given mannersubmissively, or cunningly, or aggressively, or in any combination or serial pattern. His conditioned behavior may have been realistic in respect to his "brutal father," but it will be neurotic when projected into his relations to the shop foreman, his boss or the traffic policeman. In such instances it must in part be the function of the analyst to trace back to its origin the coupling of the stimulus situation with the untoward behavior pattern.

Here a pertinent question arises: To what extent is the analyst's therapy operating as a "reconditioning" of the original "conditioned pattern"? In psychotherapy one of the least illumined chapters is that concerned with the dynamics of therapy. How the cure is effected and when it is effected are questions to which we can at best offer only partial and tentative answers. Of course, that is likewise true of other therapies. We know but little of the therapeutic dynamics of insulin, of the sulfonamides, of penicillin or of aureomycin. We know the end results, but not how those end results are achieved. In psychiatry, we speak in relation to the cure of abreaction, of transference, of a permissive atmosphere, of integration, of reintegration, of insight; these are useful and descriptive terms, but they do not

^{19.} Pavlov, I. P.: Conditioned Reflexes, translated and edited by G. V. Anrep, London, Oxford University Press, 1927, p. 302.

^{20.} Dalbiez,14 p. 70.

^{21.} Dalbiez,14 p. 83.

afford us an adequate representation of just what is taking place while the patient is "being" cured. Probably personality and the psyche are too complicated in structure and function to permit us to trace the adventures, the progressions and the effects of a psychological element or of a psychological impact insinuated into their labyrinthine patterns. For that we may need to invent psychological tracer elements, akin to the isotopes, and the equivalents also of Geiger counters. All this being so, it is still appropriate and timely to inquire how much of the psychotherapist's therapy is in effect a reconditioning of the original, i. e., pathological "conditioned pattern."

This is a question which brings into awareness a large number of related matters -and some other pertinent questions. Thus, it is implied in modern psychiatry that memory is more deeply retentive of experience and knowledge than was ever suspected. Some neurophysiologists believe that every experience leaves its indelible engram in the involved neural unit and structure.22 In the light of this belief, it is interesting to speculate on what happens to the memories and experiences, repressed or otherwise, which are involved in the engenderment of psychopathy. Are they, like the evil spirits of olden times, exorcised? Is it possible to obliterate an engram? If not, what happens then to the memory? Without pursuing this involved matter further, it seems clear that if memory cannot be extirpated and completely undone, it should be possible to add to it and thus to alter its qualities. This process is implied in the reconditioning of conditioned behavior. Pavlov and Watson have demonstrated this possibility in the laboratory, and I am convinced that the reconditioning of conditioned behavior is the modus operandi of much effective psychotherapy. How could the son of the domineering, brutal father "unlearn" his original lesson gained in experience save by "learning" in addition that not all father equivalents are domineering and brutal; that some, indeed, are kindly and tolerant.

I am sure that you must by this time have anticipated the objectives of my excursion and know it to be the premise to a plea for freer activity on the part of the therapist. Passivity plays an important role in certain phases of psychotherapy. Passivity may itself have the quality of "action," but passivity is "orthodox," and too often the refuge of the bewildered, the insecure and the indifferent therapist. Activity in therapy is looked upon askance. Yet if the propositions I advance are valid, if much of psychotherapy involves the reconditioning of conditioned behavior, then purposeful activity on the part of the therapist is not only permissible, but to be expected, and indeed required. The caveat indicated is this: The therapist's activity needs to be illuminated by previously gained insight into the dynamics of the patient's psychopathy—an insight usually won by a passive attention to the patient's complaints and recitations. Unillumined by such insight, active therapy is likely to be bumptious, and fatuous.

There can be no doubt that the technique of "free association" is among the greatest contributions which Freud made to modern psychiatry; yet it is all too often forgotten that "free association" is primarily an investigative instrument, that it initiates and makes possible effective therapy but is not in and of itself therapeutic. Schilder 28 stated:

. . . I might . . . formulate free association as a mutual effort between analyst and patient to bring the conflicts and problems of the patient into clear appearance. Thus, it is a directed effort and is based on a continuous inner activity of the analyst.

^{22.} Rignano, E.: Biological Memory, London, Harcourt, Brace & Company, 1926.

^{23.} Schilder, P.: Psychotherapy, New York, W. W. Norton & Company, 1938, p. 117.

The insight and the revelation which "free association" affords formulates in effect the therapeutic agenda which the patient, with the therapist's help, must then carry out and make operatively effective.

At this point, abrupt though it be, I must needs turn to the third of Freud's psychiatric contemporaries, Adolf Meyer. I doubt not that in the United States the influence of Meyer is as ponderable as that of Freud. Meyer was in every sense of the term a modest person. He was not "a fighter," either on behalf of his own, or against another's, point of view or theories. He was never diffuse in his thinking (though he was not particularly gifted as a speaker or writer); yet he never marshaled or organized his theories into a definitive text. He did give the name of psychobiology to his point of view, which he, in part, described as follows: "As long as there is life there are positive assets—action, choice, hope—not in the imagination but in a clear understanding of the situation, goals, and possibilities." By these positive assets, Meyer took his bearings, and by them he charted his therapeutic course.

Adolf Meyer, more sharply than any of his contemporaries, focused our minds and fixed our attention on the reality matrix, within which the sick and the well, the patient and the therapist, are fixed. Time and matter, opportunity and obligation, are of the essence of life and of living. We all muddle through as best we can, and the mark of the therapist is that he muddles a little better and, by that token, can help those who muddle a little less well. Psychotherapists of every school, but particularly Freudians, are prone to forget all this. They operate as if time, means and opportunity were nugatory items, not to be given much weight in their accounts. But that is a false estimate, one that betrays both the therapist and the patient. We need to be mindful not only of the patient's effectiveness but also of our own. That often means compromise, or, more aptly and correctly, the trimming of dogma to the dimensions of reality. Paul Schilder was a man free of preconceptions and broadly experienced in every form of psychotherapy, and I subscribe warmly to his comments on psychotherapy.

It is the important task of the physician to develop the patient's personality according to the capacities, endowments, and characteristics of the patient. He [the physician] will be better able to do so if he has the conviction that the other human being is an entity of its own and is valuable in so far as it is a definite person. . . . When the physician keeps the principle in mind that he has to respect the personality of his patient, he will not err too much. He has, furthermore, to keep in mind the specific social reality in which his patient lives. He should be further aware of the necessary limitation in his own point of view and should have, at the same time, a concept of his goals in life and the concept of the goals in life of the patient. The basic attitude in psychotherapy is that there is one human being who needs help and another human being who wants to give help. The attitude of the physician is the attitude of helpfulness and understanding. His aim is to relieve the patient from his suffering, and his conviction is that this aim can be reached by a better adaptation to the inward and outward reality, preferably by an increase in insight.²⁴

Adolf Meyer's other term for psychobiology is ergasiology. This is an esoteric, and yet a fortunate, term, since it embodies the very idea of purposeful, goal-aimed action and underscores the second major component of Meyer's teachings. Ergasiology mirrors a purposeful organism that pursues immediate objectives, strung together in a long-term, but not always appreciated, pattern or trajectory. The human organism is always moving in a patterned direction, and even when the

^{24.} Schilder,23 pp. 170-171.

overt motion is irrational and contrary to the norm pattern one can assume that the overt abnormal only overlays and masks the normal. Irrespective of age and condition, there is, as long as life persists, a momentum, albeit at times rather weak, in the direction of the fulfilment of the goals initiated in the conjunction of the gametes, from which the individual derived. This realization is a therapeutic asset. It offers leverage by which the patient can be helped to regain well-being and effectiveness. It, this realization, counterbalances the other, which dwells on the repressions, the inhibitions, the impedimenta, encountered in the past and shackling the patient. The reenforcement of goal striving can be effected at the same time as insight is gained by uncovering of repressed, conflict material. The one need not always wait on the other.

Here I must wind up my argument. I shall not recapitulate the matters presented, save only as I offer an apology for their exposition. Freud ended his autobiographic study with the following words:

Looking back over the patchwork of my life's labours, I can say that I have made many beginnings and thrown out many suggestions. Something will come of them in the future. But I cannot tell myself whether it will be much or little.

I have attempted to indicate, in broad terms, something of what has come out of the "patchwork" of Freud's labors. That "something" is enormously important. But we who are Freud's inheritors cannot rest, but, rather, must strive to advance that discipline to which he and other great and good men devoted their best years and energies. In that spirit, I roamed over a broad historical terrain and, like Montaigne, picked for you a bouquet of flowers—from other men's fields. I trust it is to your liking, and as much to your profit as it has been to mine.

I pledged you I would be in earnest, and so I have been. I am now released of my pledge, and hence may offer in levity one account for the title "Psychiatry Without Freud." It is told of a man who called his wife his better seven-eighths that, when asked why the fraction, he answered: "Oh—that's just to keep her from thinking she is the whole of it."

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Abstracts from Current Literature

Anatomy and Embryology

An Experimental Analysis of Some Factors Involved in the Development of the Fissure Pattern of the Cerebral Cortex. Donald H. Barron, J. Exper. Zool. 113: 553 (April) 1950.

Observations on the brains of near-term fetal sheep, of which selected portions were destroyed through intrauterine surgery before or at about the time of the appearance of the first fissures (about 73 days after insemination), demonstrate that the folding of the cortex of the cerebrum is not due to a disproportion between (1) the rate of increase in the capacity of the cranial cavity and the mass of the cerebrum or (2) the rate of increase of the cortical surface relative to the underlying structure of the telencephalon and the diencephalon.

The results were most striking in the case in which a twin sheep served as control. The heads of the two fetuses were similar in size and shape. The two hemispheres of the fetus operated on had been completely separated (the corpus callosum was absent, and the optic chiasm and floor of the third ventricle were missing), but some of the thalamus tissue and the posterior portion of the basal ganglia were left. Despite these great changes in volume and capacity of the structures underlying the cerebral cortex, the anteroposterior and the transverse dimensions, as well as the heights of the hemispheres, were almost identical with the controls. The cortex of the hemispheres was convoluted, although the pattern of the sulci resembled that of a normal fetus about 30 days younger. The cerebellum was small, probably because of the destruction of the cerebral peduncles.

These observations appear to justify the inference that the forces primarily responsible for cortical folding are resident in the cortex. However, the possibility must be recognized that these primary forces may be modified by the growth of cells outside the cortex.

REID, New Brunswick, N. J.

Some Connections of the Orbito-Fronto-Temporal, Limbic and Hippocampal Areas of Macaca Mulatta. K. H. Pribram, M. A. Lennox and R. H. Dunsmore, J. Neurophysiol. 13:127 (March) 1950.

The authors investigated some of the connections of the rhinencephalic and limbic areas of Macaca mulatta monkeys by means of the technique of physiologic neuronography, in an attempt to extend reports of previous studies.

The following areas can be recognized by differences in their firing patterns: trigonal, subcallosal and medial orbital; precallosal cingulate; supracallosal anterior cingulate; supracallosal posterior cingulate; retrosplenial, posterior orbital and anterior insular; temporal polar; periamygdaloid, and entorhinal. An attempt was made to correlate these with cytoarchitectural differences and with the subcorticocortical connections whenever possible. Some of the connections of the hippocampus and the amygdala were also investigated.

The corticocortical interconnections of these areas suggest that they fall into three groupings:

1. The trigonal, subcallosal and medial orbital, precallosal singulate, posterior orbital and anterior insular, temporal polar, periamygdaloid and entorhinal areas are heavily interconnected; this group may be referred to as the orbitofrontotemporal region.

2. The second group includes the projection areas of the three divisions of the anterior thalamic nucleus. There are three of these areas: supracallosal anterior cingulate, posterior cingulate and retrosplenial. According to previous studies, these areas are closely related to the cortex surrounding the cingulate sulcus and to certain aspects of the lateral surface of the hemispheres. They are functionally interconnected by extremely short fiber systems. This group may be referred to as the limbic region.

3. Finally, the consideration of the hippocampal formation as a separate region is tentative until its relation to the orbitofrontotemporal and the limbic areas is further clarified and any possible connections with the lateral neocortex are investigated.

ALPERS, Philadelphia.

A STUDY OF EFFERENT CONNEXIONS OF THE FRONTAL LOBE IN THE HUMAN BRAIN AFTER LEUCOTOMY. M. MEYER, Brain 72:20, 1949.

Margaret Meyer studied with sliver stains the brains of four patients who died within seven to 16 days after leukotomy, in an effort to trace fibers which arise in the frontal cortex to their termination in the subcortical nuclei. She found that fibers from the severed areas terminated in the dorsomedial nucleus of the thalamus after all the leukotomy lesions, including those restricted to the frontal areas. When the lesion extended into the white matter underlying the dysgranular and agranular cortex of the frontal lobe (rostral part of area 6, area 8 and the posterior portion of area 9), terminal degeneration was present in the dorsomedial and ventro-lateral thalamic nuclei, mamillary body, globus pallidus, zona incerta, Forel's field, red nucleus and subthalamic nucleus. She was unable to demonstrate a projection from the rostral cingular gyrus to the anterior nucleus of the thalamus. After lesions anterior to the precentral cortex there was degeneration of fibers of the frontopontile tract in the medial portion of the peduncle.

FRANKEL, Philadelphia.

Physiology and Biochemistry

ANOXIA AS A CAUSE OF FETAL DEATH AND CONGENITAL DEFECT IN THE MOUSE. T. H. INGALLS, F. J. CURLEY and R. A. PRINDLE, Am. J. Dis. Child. 80:34 (July) 1950.

That anoxia at critical stages of prenatal development is an important cause of acquired malformations of the fetus is an inference derived from earlier studies by Ingalls on mongolism, retrolental fibroplasia and tracheoesophageal fistula. The authors have tested this hypothesis experimentally by submitting pregnant mice at various stages of gestation to rarefied atmospheres.

Ingalls and his co-workers found that maternal anoxia may result in fetal death or congenital deformity in the mouse. The effect on the conceptus varies with the degree of maternal-placental anoxia and the stage of gestation at which the anoxic insult occurs. The effect registered on the fetus is determined also by anatomic characteristics of the site at which localized cellular damage occurs, and the hypothesis is advanced that rapidly differentiating tissues are more vulnerable to anoxia than resting or fully differentiated cells.

Alpers, Philadelphia.

Functional Significance of Residual Sympathetic Pathways Following Verified Lumbar Sympathectomy. W. C. Randall, W. F. Alexander, A. B. Hertzman, J. W. Cox and W. P. Henderson, Am. J. Physiol. 160:441 (March) 1950.

Relapse of patients following sympathetic denervation has been variously attributed to nerve regeneration, sensitization of blood vessels to humoral agents, development of intrinsic tone in vessels and incomplete denervation. Of these possibilities, the last constitutes the subject of this study.

Carefully controlled observations in the trained, unanesthetized dog are reported on peripheral vasomotor and sudomotor activity and temperature responses following verified complete removal of the lumbar portion of the sympathetic trunk. Precise anatomic and histologic analysis of the spinal nerve roots is correlated with the functional studies. Immediately after operation, relatively high blood flows and surface temperatures were usually observed in the pad of the hindpaw. Within two to seven days decreasing flows indicated a remarkable recovery of vascular tone. Positive, though frequently reduced, sweating responses were observed in all animals at various intervals after operation.

The existence of accessory vasoconstrictor pathways after a complete lumbar sympathectomy was demonstrated by two series of observations: 1. Direct faradic stimulation of the tibial and peroneal nerves induced strong vasoconstrictions in the foot pads. 2. Procaine blockade of these nerves resulted in prompt vascular relaxation with high blood flow levels. The recovery in tone after operation may be related to these accessory fibers. A possible anatomic basis for these observations may be inferred from the fact that serial sections of the spinal nerves and their intercommunicating rami in the lumbar segments taken at autopsy from the animals operated on revealed ganglion cell aggregates (with some variation from animal to animal) in relation to

ventral primary divisions of the second, third, fourth and sixth lumbar nerves. The postganglionic fibers of these cells apparently pass directly along the ventral primary ramus of the spinal nerve without entering the paravertebral ganglion chain. They would not be interrupted by lumbar ganglionectomy.

ALPERS, Philadelphia.

PILOCARPINE SENSITIZATION IN THE PARASYMPATHETICALLY DENERVATED PUPIL OF THE CAT. E. A. NEIDLE, Am. J. Physiol. 160:467 (March) 1950.

In this investigation the response of the cat's pupil to topically applied and intravenously administered pilocarpine was studied at various times after ciliary ganglionectomy.

Neidle found that removal of the ciliary ganglion in the cat produces extreme sensitization of the sphincter of the iris to pilocarpine nitrate, given either by vein (0.4 mg. per kilogram of body weight) or instilled directly into the conjunctival sac (0.01 to 0.04 mg. per eye). Sensitization of the pupil to threshold doses of pilocarpine, given systemically or topically, occurs immediately after removal of the ciliary ganglion but is not maximal until five or eight days after denervation. When supramaximal amounts of pilocarpine nitrate (0.04 to 0.4 mg. per eye) are administered topically, sensitization is maximal 24 hours after denervation. Intravenous injection of four to six doses of pilocarpine results in a decrease of 50 per cent or more in the sensitivity of the pupil. Repeated intravenous injection of the drug does not alter the development of sensitization in a pupil on which subsequently parasympathetic denervation is carried out. Repeated local application of pilocarpine does not alter the sensitivity of the denervated pupil to the drug, nor is sensitivity to topically administered pilocarpine depressed by previous intravenous injections. There is a slight but gradual decrease in the sensitivity of the denervated pupil to pilocarpine, given either systemically or locally, with the passage of time. The decrease is apparent as early as 35 days after denervation. Sensitivity reaches minimum levels at some time after the two-hundredth day and then tends to remain constant.

ALPERS, Philadelphia.

Experimental "Allergic" Encephalomyelitis: II. On the Nature of the Encephalitogenic Agent. C. E. Lumsden, Brain 72:517, 1949.

Lumsden reports on his investigations into the nature of the encephalitogenic factor in brain tissue which is responsible for the lesions of experimental allergic encephalomyelitis. Guinea pigs were used in this series. The animal tissue was homogenized in an adjuvant base consisting of I part isotonic sodium chloride solution with 1 per cent phenol, 1 part hydrophilized wool fat (eucerin®) and 2 parts liquid petrolatum containing heat-killed tubercle bacilli; the mixture was heated to 65 C. for one hour. Injections were given into the abdominal wall every week for several weeks. His studies resulted in the following conclusions: Allergic encephalomyelitis can be produced by either heterologous or homologous brain preparations, but homologous preparations are more efficacious. When human brain is injected, encephalitogenic material is present in both the gray and the white matter; hence this factor is not limited to the myelin. The encephalitogenic factor is not inactivated in guinea pig brain tissue by autoclaving and treatment with dilute solution of formaldehyde, or by treatment with acetone, alcohol, ether or chloroform. It can be extracted, along with sphingomyelin and cerebrosides. Tissues other than brain and peripheral nerve treated with adjuvants are without encephalitogenic effect. Lumsden believes that the active factor is a chemical substance which when administered with adjuvants becomes antigenic. Since adjuvants with tissue other than brain will immunize guinea pigs against allergic encephalomyelitis, it is inferred that the essential immunizing factor is resident in the adjuvant alone and that the immunity findings are due to this cause.

FRANKEL, Philadelphia.

Phenomenon of Tactile Inattention with Special Reference to Parietal Lesions. M. Critchley, Brain 72:538, 1949.

Critchley reviews the phenomenon of tactile inattention. He is of the opinion that "tactile inattention" is synonymous with the "tactile extinction" of Bender and his co-workers but takes exception to the term "extinction," since he feels that a deficiency in attention is conspicuous in

these subjects and may play the responsible role. He explains tactile extinction associated with cerebral lesions on the basis of rivalry between two contending stimuli; the stimulus applied to a body segment of high perceptual threshold is distracted by another stimulus synchronously applied to a segment of lower threshold. In these circumstances, extinction is due to a deficit in attention. In addition, when the subject opens his eyes and focuses his attention, he perceives the stimulus on the affected side.

Tactile inattention has oftenest been described with cerebral lesions which tend to invade the parietal lobe deeply. It has also been observed with lesions of the spinal cord and with cerebral lesions outside the parietal lobe, but in cases of the latter considerable intellectual confusion has been present.

FRANKEL, Philadelphia.

ON SPATIAL SUMMATION OF SENSORY STIMULI IN MAN. J. D. FORTUYN, Brain 72:562, 1949.

When the point of a pin is dragged across the surface of the skin, the sensation of pain is gradually increased. This is probably due to summation of stimuli, since during the stroke a number of points closely related in space are stimulated one after the other. The change is more pronounced if axial lines are passed; e. g., the dermatomes of the fifth cervical and the second thoracic spinal nerves touch each other on the skin surface of the inner side of the upper arm. This phenomenon is brought out more clearly when there is diffuse impairment of the peripheral nerves or the posterior column. After transection of the spinothalamic tract or after tractotomy, the contrasts are abolished, although the pinprick is felt. These observations have been explained on the basis of spatial summation taking place in the cord. Certain forms of hyperesthesia, although eventually conditioned by processes set up in the peripheral nerves, are founded on spinal mechanisms.

FRANKEL, Philadelphia.

ON THALAMIC DYSESTHESIAS AND THEIR SUPPRESSION BY BILATERAL STIMULATION, R. A. HENSON, Brain 72:576, 1949.

Henson reports on a patient who had a thalamic syndrome affecting the left half of his body. Stimulation of the left arm, leg and side of the trunk with pinprick, heat or cold produced characteristic dysesthesias. Simultaneous bilateral stimulation with the same stimuli resulted in suppression of the unpleasant and painful sensations on the left half of the body. Only the stimulus on the normal (right) side was appreciated.

Necropsy revealed a spongioblastoma multiforme involving the right parietal region and invading the basal ganglia. There were severe damage to the right thalamus and complete interruption of the sensory fibers running between the sensory receptor nuclei of the thalamus and the right parietal cortex; but the dorsomedial nucleus of the thalamus was intact, and some cells were present in the lateral nuclei.

Henson postulates two pathways for the awareness of dysesthesias in the thalamic syndrome. When the destruction of the lateral nucleus is incomplete, pain impulses may still be transmitted by the lateral nucleus; but the pattern of excitation is disarranged, and a disorderly series of impulses reaches the dorsomedial nucleus, frontal lobe and parietal cortex. The pain impulses reaching the lateral nuclei are relayed to the postcentral gyrus and also to the dorsomedial nucleus, which projects to the frontal cortex. Hence the dysesthesias in this patient may have reached consciousness in the frontal lobe as an alternate route. The sensory suppression of the dysesthesias on bilateral stimulation is explained by the fact that the patient showed decreased awareness of the left half of his body. When the opposite side was stimulated, it captured all the patient's attention, severing the hold of the left side on consciousness.

FRANKEL, Philadelphia.

DELAYED WITHDRAWAL REFLEX AND PERCEPTION OF PAIN: STUDIES IN A CASE OF SYPHILITIC MENINGOMYELITIS AND TABES WITH EXTENSOR PLANTAR RESPONSES OF A TYPE NOT PREVIOUSLY DESCRIBED. M. ASHBY, Brain 72:599, 1949.

Ashby describes a patient with syphilitic meningomyelitis and tabes whose extensor plantar response showed a double component; the delayed pain perception was associated with a delayed withdrawal reflex of the paralyzed legs. When the skin of the distal part of either foot was

punctured by a pin, the patient noted the sensation of sharpness, but not of pain. The initial response was rapid and isolated dorsiflexion of the great toe, which persisted about one second. After the great toe had returned to its neutral position, a second severe pain, cramplike in character, was felt after an interval of 0.5 to 3.5 seconds. Synchronous with the onset of the pathologic pain was a delayed flexor withdrawal reflex which involved the hip, knee and ankle, but dorsification of the great toe took no conspicuous part. A cardinal feature of the delayed pain was its prolonged duration; the longest period in the study was 11.2 seconds. The double response appears to be due to the reception of two consecutive nociceptor stimuli carried, respectively, by fast and slow pain fibers.

Frankel, Philadelphia.

The Cross-Sectional Area of Peripheral Nerve Trunks Occupied by the Fibres Representing Individual Muscular and Cutaneous Branches. S. Sunderland and G. M. Bedbrook, Brain 72:613, 1949.

Sunderland and Bedbrook investigated the cross-sectional area of the funiculi devoted to the individual muscular and cutaneous branches of the radial, median, ulnar and sciatic nerves. The area of each funiculus is accepted as an indication of the number of its constituent fibers in the nerve trunk. The influence of this factor on regeneration following suture of the divided ends of the nerve is considered. The prognosis regarding recovery of function is better when the fibers of a branch are numerous and when they are well localized within the nerve trunk.

FRANKEL, Philadelphia.

FUNCTIONAL CAPACITY OF THE ISOLATED HUMAN SPINAL CORD. R. A. KUHN, Brain 73:1 (March) 1950.

Kuhn analyzed in detail the reflex patterns elicited below the level of transection in 29 patients with complete transection of the cord at levels ranging from the second to the twelfth thoracic segment. The duration of the lesion was at least two years. Reflex activity in these cases progressed characteristically through the stages of spinal shock, minimal reflex activity, flexor spasms and alternating flexor and extensor spasms. In long-surviving patients with no complications the typical final outcome was predominantly extensor activity below the region of the injury. Spinal shock is characterized as a state of total abolition of all tendon reflexes below the level of the transection, with complete flaccidity, and paralysis of the bladder; in general, this period lasts from one to six weeks. Four men continued in this state during the entire period of study, their condition being attributed to a complicating factor, in addition to the complete transverse lesion. During the stage of minimal reflex activity, responses, usually involving distal musculature, were obtained by nociceptive plantar stimulation, but not by stimuli of a proprioceptive nature; there was a wide variation on the number of days preceding the development of well marked flexor activity. A complete flexor response or some fraction, thereof could be elicited constantly in each of the 22 men who had survived transection of the cord for long periods. The semimembranosus muscle showed consistently the most powerful reflex response; the iliopsoas muscle invariably showed strong contraction. There were two zones of low threshold from which a flexor response could be elicited most readily, i. e., the foot and genital zones (frenulum); nocuous stimuli in the form of cutaneous stimulation of the plantar of the foot was most effective, but innocuous stimulation of the plantar surface also produced flexor activity. In the genital zone, only nocuous stimuli were effective. The typical uncomplicated final outcome was predominantly extensor activity below the level of the lesion.

The movements of extensor muscles become evident as early as six months after injury, but only after the paralyzed limb had become capable of responding to an adequate stimulus with a complete response of triple flexion. Proprioceptive stimuli were most effective in the production of reflex extensor activity below the level of division of the cord; sudden stretch of the iliopsoas muscle was an especially strong stimulus.

The capacity to attain reflex penile erections were present in all men who possessed any reflex activity below the level of transection of the cord; erections did not occur in the chronically flaccid men. The focal reflexogenous zone for erection was a small area at the penile

frenulum and glans; the effective stimulus was gentle friction. None of the patients experienced a specific sensation by which they were able to recognize a penile erection. Ejaculation, as differentiated from seminal emission, was not observed.

Hyperactive tendon reflexes below the level of cord division associated with Babinski reflexes in response to plantar stimulation were present in all but the four chronically flaccid men.

FRANKEL, Philadelphia.

MECHANISM OF COUP-CONTRECOUP INJURIES OF THE BRAIN. C. B. COURVILLE, Bull. Los Angeles Neurol. Soc. 15:72 (June) 1950.

Courville restates briefly the problem of the mechanics of cerebral injury, points out the essential characteristics of coup-contrecoup lesions of the brain, reviews the contribution made by experimental investigation and analyzes the conclusions drawn from these studies.

He finds that the evidence thus far available does not disprove the clinical impression that such injuries are produced by the impact of the moving head against some immobile object. It does appear that application of force to the lateral aspect of the head may result in some contusions through shearing stresses. Certain central lesions (hemorrhages) may also be accounted for on a similar principle. There is, furthermore, reason to conclude that the subfrontal and anterior temporal contusions, so typical of the coup-contrecoup mechanism, may be explained not on the basis of movement of these parts but on the inability of the regional convolutions to move over the interior of the skull, thus dissipating the effects of force. Final conclusions cannot be made before additional experimental work is available.

Alferra, Philadelphia.

ACETLYCHOLINESTERASE: VIII. DISSOCIATION CONSTANTS OF THE ACTIVE GROUPS. I. B. WILSON and F. BERGMANN, J. Biol. Chem. 186:683, 1950.

The dependence of enzymatic activity on the pH is interpreted in terms of acidic and basic groups at the active site. Equations based on this representation are derived and applied to accurate measurements of pH and substrate dependence of acetylcholinesterase activity. The following constants were obtained: (1) the apparent dissociation constant of the enzyme-substrate complex, $K_1 = 2.6 \times 10^{-4}$; (2) the ionization constant of the conjugate acid of the basic group, $pK_{EH2} + 7.2$; (3) the ionization constant of the acid group, $pK_{EH} = 9.3$.

PAGE, Cleveland.

GLUTAMIC ACID DECARBOXYLASE IN BRAIN. EUGENE ROBERTS and SAM FRANKEL, J. Biol. Chem. 188:789, (Jan.) 1951.

Roberts and Frankel have previously reported large amounts of γ-aminobutyric acid in the brain and have shown the existence of an enzyme which can form this compound from glutamic acid. The presence of glutamic acid decarboxylase in mouse brain is reported. The activity was demonstrated in homogenates and acetone powders. The enzyme behaved like a typical decarboxylase, requiring pyridoxal phosphate as coenzyme and being inhibited by semicarbazide and hydroxylamine. Conditions for assay are described in which the reaction is of zero order and the activity is proportional to the quantity of enzyme employed.

PAGE. Cleveland.

Influence of Frontal Topectomy on Gastric Secretion: Review of Data on Twentyfour Cases and Fourteen Controls. M. B. Carpenter, J. Nerv. & Ment. Dis. 113:52 (Jan.) 1951.

For 24 topectomized and 14 control psychotic patients the total acidity and free and combined hydrochloric acid of the gastric contents and their response to the insulin Rehfuss test were determined. The topectomized patients showed no significant differences in their responses as compared with the control group. One patient who had had a topectomy of area 11 was found to have an alteration in the gastric acidity, so that, whereas he had 34 degrees of free hydrochloric acid before operation, he was achlorhydric after operation.

Berlin, Chicago.

Selective Destruction of Large Motoneurons by Poliomyelitis Virus: II. Size of Motoneurons in the Spinal Cord of Rhesus Monkeys. Robert Hodes, Samuel M. J. Peacock and David Bodian, J. Neuropath. & Exper. Neurol. 8:400 (Oct.) 1949.

The authors studied the size and distribution of the motoneurons of the anterior horns of six normal monkeys and of three animals in the chronic stage of experimentally induced poliomyelitis. They found that spinal cords from the infected animals showed a greater proportion of small neurons and a smaller proportion of large cells than did normal cords. The relative preponderance of small motoneurons and the paucity of large nerve cells increased with the severity of the lesion.

The authors believe that the abundance of small motor cells and the scarcity of large motoneurons is due to the fact that the virus of poliomyelitis first singles out for destruction the large motoneurons of the population and leaves relatively intact the small cells. As the disease process increases in intensity, small motoneurons are also destroyed.

This selection for destruction of large neurons in preference to small ones is known to occur in other pathologic processes, e. g., amyotrophic lateral sclerosis (Wohlfart and Swank) and chronic thiamine deficiency (Swank). Simple physical changes and mechanical effects, such as pressure or surgical manipulation (Hard and Lassek), are but a few of the agents whose harmful effects are seen chiefly on nerve cells of a particular size. The present study makes available additional data for the investigation of an important biologic question, namely, the fundamental basis for selective size-linked susceptibility of a neuron to a variety of diverse, harmful agents.

Alpers, Philadelphia.

RECOVERY OF SKILLED MOTOR FUNCTIONS AFTER SMALL REPEATED LESIONS OF MOTOR CORTEX IN MACAQUE. P. GLEES and J. COLD, J. Neurophysiol. 13:137 (March) 1950.

Small lesions in the thumb or hand area of the motor cortex revealed that no definite area within the internal capsule can be assigned to the corticospinal fibers coming from a particular subdivision of area 4. Moreover, small lesions in the hand area caused degeneration down to the lumbar region, suggesting that subdivisions of area 4 connect with several spinal levels.

It was found that small lesions of area 4 produced contralateral paralysis and inability to perform a delicate skilled motor act, such as opening a puzzle box. This paralysis was followed by a considerable degree of recovery and a return of motor skill. When, after recovery, area 4 was again exposed, parts adjacent to a lesion in the hand area gave hand responses which were not detectable at the earlier operation. Undercutting of these subdivisions caused recurrence of paralysis and loss of motor skill in the previously recovered arm.

It is suggested that the motor cortex does not function as a mosaic, but has a tendency when a lesion occurs to act in a less differentiated and more primitive manner which may be made possible by the plurisegmental connections of area 4 described in these experiments.

ALPERS, Philadelphia.

THE VOLUME CHANGE RESULTING FROM STIMULATION OF A GIANT NERVE FIBRE. D. K. HILL, J. Physiol. 111:304, 1950.

It has been possible to measure an increase in radius of a single cuttlefish (Sepia officinalis) nerve fiber as the result of repetitive stimulation. The increase amounts to about $0.1\,\mu$ for 10,000 impulses.

The swelling is thought to be due to an increase in the osmotic pressure of the interior of the fiber. This is attributable partly to the exchange of sodium and potassium across the membrane and partly to the transfer of sodium chloride into the fiber. It is calculated that the sodium transferred (with chloride) is about 38 per cent of the amount exchanged. Reasons are given which make it unlikely that the increase of osmotic pressure due to "metabolic" changes within the fiber, e. g., the breakdown of arginine phosphate, is large enough to have a measurable effect.

At high rates of stimulation an initial transitory shrinkage may precede the swelling phase. The meaning of this is discussed. The relation between the length and volume of a gaint nerve fiber has been investigated. If the fiber is under low tension, the length increases when the volume is raised by immersion in a dilute solution; when the tension is higher, the length decreases when the volume is increased.

A study has been made of the kinetics of the water exchange across the fiber membrane resulting from a change in the external osmotic pressure. The half-time of the process in the single fiber of Sepia or Loligo is about 1.1 min.

Thomas, Philadelphia.

HYPOTHALAMIC CONTROL OF THE ANTERIOR PITUITARY GLAND AND BLOOD LYMPHOCYTES. J. DE GROOT and G. W. HARRIS, J. Physiol. 111:335, 1950.

Electrical stimulation of the posterior region of the tuber cinereum or of the mamillary body of unanesthetized, unrestrained rabbits resulted in a lymphopenia which was similar in time relations and magnitude to that following an emotional stress stimulus. Cervical sympathectomy did not abolish this response. Electrical stimulation of certain other regions in the hypothalamus (including the supraopticohypophysial tract), or of the pars tuberalis and zona tuberalis, the pars distalis, the pars intermedia, or the infundibular stem of the pituitary gland did not elicit the response.

The lymphopenic response which follows an emotional stress stimulus in normal rabbits was abolished by lesions in the zona tuberalis (two cases) and in most cases was abolished or diminished by transverse lesions in the posterior region of the tuber cinereum or in the mamillary body. Similar lesions in the pars distalis and pars intermedia and lesions which interrupt the infundibular stem were compatible with normal responses.

The conclusion is drawn that secretion of the anterior lobe of the pituitary (probably the adrenocorticotropic hormone) is under neural control via the hypothalamus and the hypophysial portal vessels of the pituitary stalk.

Thomas. Philadelphia.

Potassium and Neuromuscular Transmission. J. Hajdu, J. A. C. Knox and R. J. S. McDowall, J. Physiol. 111:382, 1950.

Extra potassium first increases and, in large doses, then depresses the excitability of muscle at body temperature in Krebs's solution (J. Physiol. 108:502, 1949).

At room temperature neuromuscular transmission is depressed by extra potassium, and eventually a neuromuscular block is produced, which, like that produced by curare, can be antagonized by more rapid stimulation.

The depression of the muscle is enhanced by denervation, and it is suggested that the acetylcholine liberated normally antagonizes potassium depression.

THOMAS, Philadelphia.

ELECTROMOTIVE ACTION OF ACETYLCHOLINE AT THE MOTOR END-PLATE. P. FATT, J. Physiol. 111:408, 1950.

The origin of the depolarization which acetylcholine produces at the motor end plates of muscle fibers is discussed. One of the suggested mechanisms which requires an increase in the sodium permeability of the end-plate membrane is subjected to experimental test.

When frog muscle is kept in sodium-free solutions, acetylcholine in concentrations of 10⁻⁷ and 10⁻⁵, although not eliciting any visible mechanical response, still produces a local depolarization at the end plate.

The pesence of sodium increases the depolarization produced by acetylcholine and leads to the setting up of propagated impulses. Sodium in concentrations below that necessary for propagated impulses already exerts a pronounced effect on the magnitude of the local depolarization.

The quantitative relation between acetylcholine concentration and end-plate depolarization is investigated in the absence of sodium. Its theoretical significance is discussed from the point of view that the depolarization may be due to a direct penetration of the end-plate membrane by A. Ch., ions.

Thomas, Philadelphia.

CIRCULATORY CHANGES IN THE FOOT AFTER LUMBAR SYMPATHECTOMY. R. B. LYNN and H. BARCROFT, Lancet 1:1105 (June 17) 1950.

Lynn and Barcroft measured the blood flow in the feet and the temperatures of the toes of 19 limbs before and after lumbar sympathectomy. Six of the patients had normal arteries, four of them having hyperhidrosis and two deep venous thrombosis. Of the 13 patients with varying degrees of arterial abnormality, two had acrocyanosis, two had chilblains and varicose veins, one had a popliteal aneurysm, two had chilblains and ulceration and six had diffuse obliterative arteritis or arteriosclerosis.

The average blood flow in the six patients with normal arteries was much increased after sympathectomy, reaching a maximum on the second day. By the sixth day vascular tone had partially recovered, and had still further returned one to three months after operation. The toes of these patients remained permanently warm after operation.

The blood flow in the patients with abnormal arteries increased after operation, but not as greatly as in the patients with normal arteries, and returned to about twice the normal. The

toes also remained warm.

The beneficial effects of sympathectomy may be considered from two standpoints: 1. In acute emergencies it tends to produce a large vasodilatation, lasting a few days. 2. In chronic cases the benefits are probably due mainly to isolation and protection of the sympathectomized vessels from strong central stimulation excited by cold and other factors. In such circumstances, the circulation in a normally innervated foot may become very small indeed, and that through a sympathectomized one is likely to be many times as great as normal.

Manow, Philadelphia.

Neuropathology

HYPOTHALAMIC LESION CAUSED BY BOECK'S SARCOID. A. GJERSE and K. KJERULF-JENSEN, J. Clin. Endocrinol. 10:1602 (Dec.) 1950.

Gjerse and Kjerulf-Jensen report on the clinical and pathologic findings in a patient aged 29 who at the age of 17 had histologically verified choroiditis associated with sarcoidosis. Ten years after the onset a change was noted in personality, characterized by fretfulness, apathy and unprovoked emotional outbursts. In the last few months of the patient's life there was excessive sleepiness, followed later by insomnia, diabetes insipidus, hyperthermia alternating with hypothermia, asthma and auricular flutter. Study of the brain post mortem revealed sarcoidosis involving only the hypothalamic area; the pituitary gland was not affected.

FRANKEL, Philadelphia.

Brains from Streptomycin-Treated Cases of Tuberculous Meningitis. G. Payling Wright and R. J. W. Rees, Proc. Roy. Soc. Med. 41:456 (July) 1948.

Examinations of the brains and spinal cords from three children, aged 30 to 34 months, who died of tuberculous meningitis revealed similar pictures. Each patient had received eight to nine weeks of treatment with streptomycin intramuscularly and intrathecally before death and had shown a progressive decrease in the number of cells in the cerebrospinal fluid. Primary lesions were found in the lungs in each case. There was a thick, yellowish, gelatinous exudate, most pronounced in the interpeduncular fossa, containing large numbers of tubercle bacilli. These organisms were found to be sensitive to streptomycin. Each brain showed a considerable degree of symmetrical hydrocephalus.

Berry, Philadelphia.

Psychiatry and Psychopathology

Precocious Sexual and Somatic Development in Boys Due to Constitutional and Endocrine Factors. W. W. Engstrom and P. L. Munson, Am. J. Dis. Child. 81:179 (Feb.) 1951.

Clinical and laboratory data are presented on a family in which the father and two sons showed precocious genital and somatic growth. Another son showed no abnormality. The term "consti-

tutional" precocious development appears to be applicable to these cases. Another boy, who also was precociously developed but who had overactivity of the adrenal cortex, was similarly studied.

Examination of the sequence of the appearance of maturity phenomena revealed that in these boys the general picture of growth in height and weight was like the adolescent "spurt" in growth of normal boys except for its occurrence at an abnormally early age. This suggests that the skeletal and probably the muscular systems respond in a fundamentally uniform manner, whether stimulated to accelerated growth by normal or by variously abnormal influences. Further, there seemed to be a relatively harmonious overgrowth of the skeletal and muscular systems. In the boys who suffered from the "constitutional" disorder, pubic hair growth rapidly assumed adult characteristics, as in normal boys, during the period of maximal increments in height and during maximal growth of the testes and penis. The bone age of these boys was concomitantly advanced. However, harmonious acceleration in the appearance of other phenomena of maturity, which would have been expected in normal boys of comparable biologic age, was not present. The following discrepancies were noted: The 17-ketosteroid excretion was considerably below that which would be expected for their "biologic" age; the appearance of axillary and facial hair was delayed; dentition was not advanced, and the boys exhibited no pubescent personality or behavior.

The findings on theses boys and on the boy with the adrenogenital syndrome suggest that in these circumstances their pubic hair, and possibly their axillary hair, growth was not necessarily conditioned by adrenal cortical activity. It was not possible to correlate their 17-ketosteroid excretion with their degree of physical maturity. In general agreement with other investigators, Engstrom and Munson found that the teeth and the central nervous system apparently are peculiarly invulnerable to those influences which cause precocious development in other areas.

ALPERS, Philadelphia.

MENTAL ACHIEVEMENT OF CONGENITALLY HYPOTHYROID CHILDREN: A FOLLOW-UP STUDY OF TWENTY CASES. A. TOPPER, Am. J. Dis. Child. 81:233 (Feb.) 1951.

There is considerable evidence to show a lack of correlation between mental results obtained in the child with congenital hypothyroidism and adequacy of therapy. This discrepancy is ascribed to such causes as the degree of deficiency of the gland, the innate mental endowment and—what seems to be the most significant factor—impairment of the brain, existing in the cretin either as a primary amentia or as a developmental result of lack of thyroid stimulation.

Topper in this paper had a twofold purpose: (1) to present the results of a review of data on 20 cretins who have been followed for one to 25 years, and (2) to report on the electroencephalographic findings in 13 of this group.

Thyroid U. S. P. was used for all patients. The most satisfactory dose was found to be that required by the individual cretin for his physical progress. There was a good correlation between thyroid therapy and physical skeletal and sexual development in all the children.

Of all the 20 patients, 8 have remained mentally defective, and 1 functions within the borderline of normal intelligence, while 11 have attained normal intelligence, 2 being within superior normal range. Two children were excluded because of unsatisfactory treatment, leaving 7, or 39 per cent, of the study group definitely feebleminded. In an effort to investigate a possible cerebral defect in these patients, electroencephalographic studies were made. Five of these cretins (80 per cent) showed electroencephalographic tracings that revealed "diffuse cerebral dysfunction." Electroencephalographic studies made as a control in six of the cretins who had reached a normal level of intelligence showed tracings that were entirely consistent with normal mentality.

From her findings Topper concludes it can be proved by direct investigation of the brain by the electroencephalogram that a cerebral defect explains the mental deficiency of adequately treated cretins. When such studies are made in infancy, they can be of significant prognostic import, since no amount of thyroid can bring about normal mentality in the presence of cerebral dysfunction, whereas if the electroencephalogram shows a normally functioning brain, adequately pursued therapy can bring about normal mentality, even in a child with congenital hypothyroidism.

ALPERS, Philadelphia.

THEORETICAL ASPECTS OF FRONTAL LOBOTOMY AND SIMILAR BRAIN OPERATIONS. P. H. HOCH, Am. J. Psychiat. 106:448 (Dec.) 1949.

Hoch points out that frontal lobotomy and similar operations which interrupt cortical connections have a certain specificity and cannot be replaced by any brain operation. To achieve therapeutic results, it is necessary to remove a certain amount of cortex or to interrupt a certain number of corticothalamic connections. If not enough pathways are cut or not enough cortex is detached, improvement will not result. If too much cortex is damaged, rather marked personality damage is produced.

Frontal lobotomy is performed on mentally well integrated persons who suffer from intractable pain. The alteration in the pain experience after operation is the most important one. Formerly the pain dominated the patient. After the operation he still is conscious of pain; the perception of it is unchanged, but he is not concerned with it. The dominance is eliminated, and the patient can turn his ego function elsewhere.

Hoch concludes from these observations that there exist a primary postoperative awareness of sensory stimuli and a secondary integrative awareness which incorporates sensory stimuli into the ego. He believes that these observations made in cases of intractable pain give a clue to changes seen in patients with mental disease who have undergone frontal lobotomy. The patient's behavior toward his symptoms is very similar to that observed in patients with intractable pain. At first he is dominated by the symptoms; the ego is defenseless and overpowered. After the operation all the symptoms are present, but the attitude of the patient toward his symptoms has changed; he can live with them.

The various lobotomy procedures damage the brain to a greater or less extent. The most damaging is the translateral form of lobotomy; somewhat less is topectomy, and least damaging is the transorbital form.

Frontal lobotomy points to a very important problem in therapy. Psychotherapy at times is able to reduce the impact of obsessive symptoms on the patient if they are not too strong. Amobarbital sodium or shock treatment reduces temporarily the pitch of this emotional domination and, in a manner of speaking, puts the patient back into his own hands. Frontal lobotomy does the same, but in a more permanent way.

Hoch believes that frontal lobotomy is not only an important tool in the treatment of clinical mental disorders but will also be of great theoretical importance.

ALPERS, Philadelphia.

Influence of Bilateral Prefrontal Lobotomy on Thyroid Activity in Psychiatric Patients. E. B. Brody, E. B. Man and B. E. Moore, J. Clin. Endocrinol. 10:716 (July) 1950

Brody, Man and Moore found no constant direction or degree of change in the level of thyroid secretion in 16 patients after prefrontal lobotomy. No relation to postoperative change was discovered with respect to the clinical features of the illness, laboratory data, physical characteristics or response to surgical therapy. In the authors' opinion, the lack of correlation between serum iodine findings and the clinical results of lobotomy suggests that the psychiatric effect of this operation occurs independently of any gross change in thyrotropic and thyroid activity of the pituitary.

Frankel, Philadelphia.

Effect of Leucotomy on Creative Personality. E. L. Hutton and M. Bassett, J. Ment. Sc. 94:332 (April) 1948.

In earlier studies of the personality alterations produced by prefrontal lobotomy, Hutton and Bassett used the Rorschach technique but found that memory of preoperative testing minimized the validity of later interpretations. Both individual administration and the Harrower-Erickson multiple choice method were used. The results indicate that leukotomized subjects show decreased originality and creativity and, though unhampered by self consciousness, are unenthusiastic and disinterested. The responses were largely conventional, evoked by large details, with human and movement responses infrequent. The majority of new responses, follow-

ing operation, were determined by color, and uncommonly by shading. These findings, coupled with clinically observed lack of initiative and a tendency to live in the immediate present, suggested a diminution in creative activity.

Further investigation has been centered on two new diagnostic instruments, a multiple choice thematic apperception test of the authors' devising and a graphic drawing test. In the first, patients who had been treated by lobotomy were very unsuccessful; in some cases, in which they showed extreme constriction of thought, no story could be produced. Such stories as were written tended to be brief, autobiographical or descriptive. In drawing, leukotomized subjects were able to copy well but showed decrease in the abilty to make an original sketch. These two techniques, therefore, were in agreement with Rorschach results in indicating a diminution in creativeness.

The talent for creating involves four factors: imagination; emotional motives and associated judgements of value; technical knowledge and practical ability; and sustained effort and persistent application. There is no gross change in the last two elements in the postleukotomy patient. There is, on the other hand, a relative lack of imagination, meaning by that term the capacity to reorganize and reintegrate images from former percepts into a new whole. This synthesis from eidolons derived through sensory experiences is the essential basis of man's creative activity and is dependent on language. A question yet to be answered is whether the lobotomized patient ceases to exercise this function because section of prefrontal fibers has destroyed the power, or because the operation has dissociated the emotional factors which normally motivate it. The absence of creativity may account for such changes as freedom from anxiety and from awareness of moral obligation. If these persons are unable or have no emotional urge to imagine a possible future or an ideal standard, they will naturally be released from worry, guilt and remorse.

BEATON, Tucson, Ariz.

Meninges and Blood Vessels

Spontaneous Subarachnoid Hemorrhage. E. F. Hurteau, J. A. M. A. 142:988 (April 1) 1950.

Hurteau reports a case of spontaneous subarachnoid hemorrhage due to rupture of a congenital aneurysm and emphasizes the value of cerebral arteriography and newer neurosurgical techniques. In spite of inadvertent rupturing of the aneurysm during its exposure, this patient made an uneventful recovery.

ALPERS, Philadelphia.

Tuberculous Otitis and Meningitis. D. I. Arbuse and E. Levenson, J. Nerv. & Ment. Dis. 113:165 (Feb.) 1951.

Of a series of 42 patients with tuberculous meningitis, two had associated tuberculous of tits media. One, a man aged 46, had chronic otologic disease of three years' duration, and one year prior to his admission the aural discharge was found to contain tubercle bacilli. He died of lymphocytic meningitis, from which tubercle bacilli were not cultured. The second patient, a girl aged 18 years, had had a draining ear for 10 years, from which tubercle bacilli were ultimately cultured. Lymphocytic meningitis developed, and pellicle and Levinson tests gave positive results. She showed improvement for one year while receiving streptomycin therapy.

BERLIN, Chicago.

Temporal Arteritis (Giant Cell Arteritis). A. P. Dick, Proc. Roy. Soc. Med. 41:379 (June) 1948.

A man aged 69, who had previously been well, complained of dull headache in the left temporal region of about five weeks' duration. Examination showed a prominent left temporal artery with absence of pulsation in the distal half and only slight tenderness. He had persistent leukocytosis (the count being as high as 24,000 per cubic millimeter) with 80 per cent neutrophils, irregular fever and increased sedimentation rate. Drowsiness, lack of interest and mental confusion developed. The spinal fluid was normal. For one day the patient had bilateral ptosis

and weakness of conjugate upward deviation of the eyes. A few days later there were urinary retention and albuminuria, with a blood urea nitrogen content of 63 mg. per 100 cc. He was treated with penicillin and gradually improved after removal of a biopsy specimen. The specimen from the left temporal artery showed degeneration of the media, with some round cell and plasma cell infiltration, adventitial infiltration with round cells and a ring of giant cells. The lumen was almost occluded by gross hyperplasia of the intima.

Berry, Philadelphia.

Diseases of the Brain

Subdural Hematoma and Effusion in Infants. Arthur R. Elvidge and Ira J. Jackson, Am. J. Dis. Child. 78:635 (Nov.) 1949.

Elvidge and Jackson present an etiologic and clinicopathologic analysis of 55 cases of subdural hematoma in infants and attempt to show the importance of maintaining an adequate fluid and protein balance as an adjunct to surgical treatment.

The authors classify these patients under four headings:

- 1. Group of Definite Birth Injuries.—Of 10 patients, six showed skull fracture, and three, tentorial tears. All had histories of difficult labor, instrumental delivery and symptoms since birth. They presented a uniform clinical picture. Spasticity was the most prevalent physical finding on admission. Seizures, focal and generalized; abnormal neurologic findings, such as pupillary signs and extraocular paresis, and respiratory difficulties each occurred in about one third of the babies. Four infants had tense fontanels; hydrocephalus was present only in the oldest (21 day old) infant. Opisthotonos was present in only three infants, but this was its greatest incidence in any one group. Ninety per cent showed bloody subdural fluid. No subdural membrane was found. Bilateral effusion occurred in eight patients. Of seven infants who died, autopsy showed diffuse subdural and subarachnoid hemorrhages in two, pericardial and pleural hemorrhages in two and tentorial hemorrhages in three. After 10 years, two survivors treated by trepanation were normal; one (after one year) who underwent craniotomy was mentally and physically retarded.
- 2. Group of Probable Birth Injuries.—This group comprised 26 patients, from 13 days to 14 months of age, admitted as chronically ill. Fourteen had a history of difficult and instrumental delivery; 11 presented signs and symptoms recognizable since birth; 3 were premature; 20 per cent were born as one of twins.

The great majority were brought to the hospital because of an enlarged head. All infants in this group had hydrocephalus. The second major symptom was seizures; 16 had a history of this disorder. Two-tenths per cent had a history of taking feedings poorly, and 26 per cent had had respiratory difficulties, which usually occurred during the first week of life. Five patients exhibited spasticity, and two opisthotonos.

Eleven showed abnormal neurologic findings of no localizing value; all these had bilateral effusion. Bilateral effusion was observed in 19, and unilateral effusion, in seven patients. All but one of those with bilateral effusion showed the same type of subdural fluid on the two sides. Xanthochromic fluid was found in 18 and bloody fluid in eight patients. The protein value of the xanthochromic fluid was from 148 to 3,390 mg. per 100 cc.; that of the bloody fluid, up to 6,000 mg. per 100 cc.

A subdural membrane was observed in 24 instances in 15 patients. The spinal fluid in seven infants was clear, colorless and of normal protein value. Two had yellow fluid with elevated protein content, and one (15 days old) had bloody fluid. Five infants died after operation, a mortality rate of 19.2 per cent. Fourteen have been followed from six months to six years. Seven are normal. Seven showed mental retardation and some neurologic deficit.

3. Groups with Postnatal Head Injuries.—Nine patients, aged 2 to 30 months, had a history of severe postnatal head injury. They had much the same clinical picture as that of an adult following a severe head injury. Hemiparesis, reflex changes, spasticity, respiratory difficulties, restlessness, unconsciousness, shock and a history of recent head injury were predominant observations.

Six unconscious infants underwent operation soon after admission. All had bloody subdural fluid, and there were blood clots in five. The effusion was bilateral in two patients and uni-

lateral in four patients. All these patients died within 12 hours. Autopsy revealed known subdural and subarachnoid hemorrhages, skull fractures and laceration of the brain.

The other three patients were seen two to six weeks after injury. Two had periods of unconsciousness after the injury. The third, who had sustained a skull fracture, had focal cortical seizures, and feeding trouble one week after injury. One infant, seen two years after treatment, had no mental retardation and slight hemiparesis.

4. Unclassified Group.—This group comprised 10 infants 2 months to 24 months of age with subdural effusion and no significant history, who were brought to the hospital as chronically ill. On admission they showed about the same clinical picture as that in group 2 or group 3. Hydrocephalus, seizures and paresis were most prevalent. Three infants had papilledema. This is the only group in which opisthotonos was not observed. Six had extracranial infection coincident with the onset of their seizures or paresis. The onset of symptoms was six months before admission, on the average. Several had bilateral subdural effusion; two had bloody fluid; two showed a protein content of the subdural fluid of 525 to 4,120 mg. per 100 cc.; four had a subdural membrane, and five had lumbar punctures with clear and colorless fluid and a normal protein in all but one. The total operative mortality was 20 per cent. Of four patients followed one to three years, three showed no mental retardation.

The surgical treatment consists in emptying the subdural space and completely removing the membranes when they are present. The acute subdural hematoma is best treated by aspiration, for no membrane is usually present at this early stage. The chronic subdural effusion (as in groups 2 and 4) is most satisfactorily treated after confirmation of the diagnosis by subdural tap, by trepanation for identification of membranes and, if their presence is confirmed, by early complete removal of the inner membrane. It is in these groups that membranes are commonly found. The authors believe that the complete removal of the inner membrane is most important, for it is this structure that prevents normal expansion of the brain.

Careful attention to the fluid and protein balance in the management of these infants will aid in reducing greatly the operative mortality. The authors record that the actual amount of protein and fluid lost in the subdural space may be 5 and 10 per cent, respectively, of the daily requirements of the infant. The protein lost in the subdural space, and no longer utilizable for body needs, is one reason that these infants appear pale and undernounished when seen by the physician.

Februle Convulsions in Childhood. Margaret A. Lennox, Am. J. Dis. Child. 78:868 (Dec.) 1949.

Lennox made clinical and electroencephalographic studies on 240 children with febrile convulsions. Two thirds of all febrile convulsions were found to occur in boys between 1 and 3 years of age. They almost always occur with a high fever, and one-half the children have a family history of convulsions, usually infantile or occurring in isolated cases. The electroencephalogram was normal in 71 per cent of cases. An abnormal electroencephalographic record increases the likelihood that recurrent nonfebrile convulsions or epilepsy will develop. From analysis of the electroencephalographic tracings the following conclusions are drawn: 1. An abnormally fast tracing is often correlated with a history of traumatic birth, and 50 per cent of these children had recurrent nonfebrile convulsions within a three year period. 2. An extremely slow or focally abnormal electroencephalogram suggests pathologic changes in the brain caused by febrile convulsions. 3. A paroxysmal electroencephalographic abnormality tends to occur in children with both genetic and traumatic factors predisposing to epilepsy, and 25 per cent had recurrent nonfebrile convulsions in a three year period.

ALPERS, Philadelphia.

Encephalitis in Diphtheria. V. B. Dolgopol and S. H. Katz, Am. J. Dis. Child. 79:640 (April) 1950.

Diphtheria is usually regarded as a disease affecting the cranial and peripheral nerves rather than the central nervous system. Dolgopol and Katz review the literature covering the cases in which inflammatory changes were observed in the brain or medulla on histologic examination and report five cases of inflammatory damage to the central nervous system occurring in the course of diphtheria. Clinical neurologic manifestations were present in only one case.

The damage consisted of perivascular infiltration and glial nodules in the gray and white matter of the cerebrum and medulla. Some degeneration of ganglion cells was present in the medulla, midbrain and thalamus. The myelin was intact in the brain and in the roots of the cranial nerves.

The medulla was affected in cases in which the illness was of 10 or more days' duration.

The central nervous system was probably damaged by direct action of circulating diphtheria toxin.

ALPERS, Philadelphia.

Brain Abscess and Meningitis Associated with a Pleuropneumonia-Like Organism:
Clinical and Bacteriological Observations in a Case with Recovery. T. F. Paine
Jr., R. Murray, I. Perlmutter and M. Finland, Ann. Int. Med. 32:554 (March) 1950.

In the case reported here a pleuropneumonia-like organism was repeatedly cultured from the central nervous system of a patient with an abscess of the brain and meningitis. The case is of interest because it probably represents the first in which an organism of the pleuropneumonia group was recognized in association with an infection of the central nervous system.

The patient failed to improve during treatment with sulfonamides and penicillin but recovered rapidly after the abscess was drained and streptomycin was used locally and systemically.

The organism was initially sensitive to streptomycin but became resistant to this antibiotic and persisted during the course of therapy.

ALPERS, Philadelphia.

Intraorbital Aneurysm: Case of Aneurysm of Lacrimal Artery. R. F. Heimburger, H. R. Oberhill, H. I. McGarry and P. C. Bucy, Arch. Ophth. 42:1 (July) 1949.

Heimburger and associates report that a woman aged 58 had a nonpulsating exophthalmos of the left eye, which had existed for two months. Examination revealed severe proptosis of the left eye, distention of the periorbital, conjunctival and retinal vessels, paralysis of ocular movements, blurring of the optic disk, visual acuity of 20/20 (right eye) and 20/70 (left eye), ptosis of the left upper eyelid and a small, sluggish pupil. Transcranial exploration of the orbit revealed that the exophthalmos was due to aneurysm of the lacrimal artery contained entirely within the orbit. The lesion was removed by the transcranial route. The patient was entirely well over a year after operation, with normal vision and normal ocular movements in the affected eye. The authors found reports of 68 cases in the literature in which a diagnosis of intraorbital aneurysm was made. Few of these reports contain information concerning any pathologic investigation, and in even fewer do the recorded facts indicate that a true intraorbital aneurysm was present. In the great majority of instances the diagnosis rested on clinical observations alone. In the early ophthalmologic literature it is evident that the diagnosis of intraorbital aneurysm was usually based erroneously on the finding of a pulsating exophthalmos. Reports of six cases in which an intraorbital aneurysm was said to have been visualized either at operation or at autopsy are reviewed, but in none is the diagnosis without question. Because of this lack of verified cases, criteria cannot be set up on which a differential diagnosis of an aneurysm within the orbit may be based. The case is reported as evidence that orbital aneurysm can be manifest clinically by unilateral exophthalmos without pulsation but with venous obstruction, increased intraocular tension and failing vision. I. A. M. A.

METASTASIS TO THE SKULL OF LEIOMYOSARCOMA OF THE UTERUS: REPORT OF CASE WITH SECONDARY INVOLVEMENT OF THE BRAIN. R. H. IWATA and C. B. COURVILLE, Bull. Los Angeles Neurol. Soc. 14:232 (Dec.) 1949.

Malignant growths of the uterus rarely metastatize to the skull. Occasionally carcinomas of the uterus, oftener of the cervix, metastasize to bone, and among the bones involved those of the skull may be included. Cranial metastasis from sarcomas of the female genital system seems to be even rarer.

This study is concerned with a case of leiomyosarcoma of the uterus with cranial metastasis occurring in a woman aged 61. The large solitary metastatic lesion had eroded the bone in

the left temporal fossa, penetrated the dura and invaded the left temporal lobe. Four other metastatic tumors (two confluent) had developed in the ribs. A survey of the literature disclosed two other cases, which, with the authors', suggest that the cranial metastases are usually large, solitary tumors of rapid evolution.

ALPERS, Philadelphia.

Transorbital Intracranial Stab Wounds. C. C. McClure Jr. and W. J. Gardner, Cleveland Clin. Quart. 16:118 (July) 1949.

McClure and Gardner report four cases of transorbital intracranial stab wounds, each illustrating a different clinical picture and demonstrating the vulnerability of the brain when approached through the thin-walled, funnel-shaped orbit.

Case 1 is that of a boy who had a penetrating wound through the left upper eyelid, caused by a pitchfork blade. Because of the absence of cerebral symptoms in this case, the intracranial wound might not have been suspected if there had not been leakage of cerebral fluid. The eyeball escaped injury. In case 2 the patient sustained an injury by falling face downward in a stubble field; the eyeball was pushed aside and thus escaped injury. The case serves to illustrate the fact that even an insignificant external wound may be the cause of a complete, and possibly permanent, external ophthalmoplegia. Case 3, in which the intracranial wound was caused by a large wooden splinter entering forcibly, illustrates a violent wound of the orbit which penetrated to a depth sufficient to produce hemiplegia in addition to the local ocular paralysis but in which the eyeball was not damaged. In case 4 the intracranial lesion was caused by stab wounds in the neck and left eye. The patient died, and postmortem examination disclosed a laceration of the right carotid artery and cavernous sinus.

McClure and Gardner stress the possibility of an intracranial wound in all cases of stab wounds of the eyelid. They also point out that in cases of carotid artery-cavernous sinus fistulas the carotid artery should be ligated intracranially before ligation in the neck.

ALPERS, Philadelphia.

Japanese B Encephalitis in Korea. R. L. Hullinghorst, K. F. Burns, Y. T. Choi, and L. R. Wheatley, J. A. M. A. 145:460 (Feb. 17) 1951.

An outbreak of encephalitis in epidemic proportions occurred in Korea during the summer months of 1934 and 1935. The relatively uniform clinical picture, together with the epidemic occurrence during summer months, strongly suggested the likelihood of Japanese encephalitis (type B encephalitis). Four cases of Japanese B encephalitis were observed during the summer of 1946 among American soldiers stationed in Southern Korea. A virus recovered from a patient who died was identified as that of Japanese B encephalitis. A specific diagnosis in the other nonfatal cases was accomplished by means of complement-fixation tests. Subsequent serologic surveys of native Korean and of indigenous domestic animals indicated that the virus of Japanese B encephalitis was widely disseminated in that country.

An epidemic of encephalitis occurred during the summer months of 1949 in Korea. The epidemic began during the latter part of August and lasted until the first week of October. A total of 5,548 cases were reported, with 2,429 deaths.

A clinical entity consistent with Japanese B encephalitis was observed in patients during this epidemic. Histologic examination of tissue in several cases showed diffuse nonpurulent encephalitis, characteristic of Japanese B encephalitis. A neurotropic virus was recovered from the brain in a fatal case. This agent and two others similarly obtained elsewhere were identified as the virus of Japanese B encephalitis. Serologic comparison of normal and convalescent persons further supports the Japanese B encephalitis virus origin of this epidemic.

ALPERS, Philadelphia.

Excessive Hunger as a Symptom of Cerebral Origin. W. R. Kirschbaum, J. Nerv. & Ment. Dis. 113:95 (Feb.) 1951.

Kirschbaum analyzed the clinical records and pathologic findings of 30 patients who showed excessive hunger during their illness. The conditions in which the symptoms developed

were primary and metastatic tumors of the brain, traumatic encephalopathy, senile dementia and Pick's disease, postapoplectic dementia, dementia paralytica and chronic encephalitis. In one case the excessive eating occurred as part of a psychomotor epileptic attack in a patient who also had grand mal seizures. In most of the cases the increased appetite was temporary and was followed by anorexia as the patient's condition deteriorated. In cases in which bulimia was due to diencephalic lesions there were associated polydipsia, polyuria and vasomotor and neuroendocrine disturbances. In the others, in which the appetite was increased by disturbances in the frontal lobe, there were only associated psychic and focal neurologic signs.

BERLIN, Chicago.

EPILEPSY AND ARTERIOSCLEROSIS. A. GORDON, J. Nerv. & Ment. Dis. 113:170 (Feb.) 1951.

In 12 persons who died of various "visceral causes," there developed epileptic phenomena for the first time between the ages of 57 and 68. They had experienced vertiginous attacks and transient attacks of monoparesis or hemiparesis, in addition to the seizures. There were areas of periarteritis and endarteritis in the cortex and subcortical white matter and in the overlying pia. The areas of vascular disturbance were present throughout the cerebral hemispheres, but were predominantly present over both motor areas and were thought to have contributed to the occurrence of seizures.

Berlin, Chicago.

RETINAL ARTERIAL OCCLUSION IN MIGRAINE. G. S. GRAVESON, BRIT. M. J. 2:838 (Oct. 15) 1949.

Graveson reports four cases of retinal arterial occlusion occurring with migraine and discusses nine others reported in the literature. From a study of these 13 cases, he concludes that no specific age group appears to be particularly predisposed to the development of this complication. Moreover, in this series there were no signs of local retinal or generalized arterial diseases, and there was no evidence of any possible source of emboli. Graveson believes that migraine should be considered a possible cause in those cases of retinal occlusion, occasionally encountered in practice, in which no cardiovascular disease can be demonstrated. Such cases are of interest primarily because they provide further evidence that the symptoms of migraine are the results of vasomotor disturbances in the region of the cranial blood vessels.

ECHOLS, New Orleans.

METASTATIC BRAIN ABSCESS. J. LEBEAU and M. ROSIER, Rev. neurol. 81:343 (May) 1949.

LeBeau and Rosier report the results of operation in 18 cases of metastatic cerebral abscess since 1944, when treatment by the method of total ablation and instillation of penicillin was adopted. They conclude that abscess is to be suspected when localizing neurologic signs or intracranial hypertension appears during the course of a subacute infection, particularly of the lung. Acute aseptic meningitis, or meningitis that does not clear quickly with penicillin, leads to the suspicion of abscess. Most abscesses in their series appeared in the posterior half of the cerebrum. The abscess is found via a burr hole. If it is acute, it is drained by puncture, and 20,000 to 50,000 units of penicillin is injected. However, if unequivocal improvement does not appear in 24 hours, a flap is turned and the abscess is ablated. In case of chronic or subacute abscess, immediate ablation is carried out. Penicillin treatment is continued for a few weeks afterward.

Ventriculographic examination is not made during the diagnostic stage.

The mortality by this method was 33 per cent, representing a considerable improvement over former results.

The authors feel that the incidence of neurologic sequelae is less than that with drainage. They carry out the ablation by opening the abscess widely and removing the capsule from the inner surfaces, a procedure which they feel can be carried out with impunity provided removal of the wall and infective tissue is complete.

LEGAULT, Washington, D. C.

Diseases of the Spinal Cord

EPIDEMIOLOGIC CHARACTERISTICS OF POLIOMYELITIS IN ICELAND. J. SIGURJONSSON, Am. J. Hyg. 51:109 (Jan.) 1950.

Analysis of the epidemiologic features of poliomyelitis in Iceland, as manifested since the disease was first recognized in 1904, provides, according to Sigurjonsson, an illustration of the behavior of this disease as influenced by the conditions of living, climate, ecology and environment peculiar to this far northern country. The causative virus has been able to maintain itself over considerable periods of time in this relatively isolated island population of 80,000 to 130,000, one third of which is concentrated in a single urban area and the rest scattered over a huge territory, in small communities and on farms with limited intercommunication. Moreover, the virus has become prevalent in this population during a period when transport, communication, living conditions, home hygiene and community sanitation were being steadily improved. Poliomyelitis has appeared in epidemics at intervals of about 10 years. As measured by morbidity and mortality rates, these epidemics have been severe in comparison with those in countries of Northern Europe and North America. During the inter-epidemic periods the disease has either completely disappeared or existed at a low, and probably largely subclinical, level. Cases of poliomyelitis have occurred in every month of the year but usually reach maximum numbers in the autumn. The most recent epidemic reached its peak in the winter. The age distribution has shown an interesting shift. In the earlier epidemics the highest attack rate was in children under 5 years of age. In recent years there has been a distinct shift in the distribution of cases toward older ages. In the latest epidemic the highest attack rate was reached in the 15 to 19 year age group, and a considerable proportion of cases was in adults. This shift in age distribution is more pronounced than that observed in some parts of Europe and North America. The author suggests as an alternative hypothesis the possibility that the shift in age distribution is due in part to coincident prevalence of an unidentified disease which closely resembles poliomyelitis. This might account also for the unusual (midwinter) seasonal distribution and for the extremely high morbidity rates.

Tonsillectomy and Adenoidectomy and Poliomyelitis. A. H. Miller, Arch. Otolaryng. 53:160 (Feb.) 1951.

In an attempt to determine whether there is any relationship between a recent tonsillectomy and adenoidectomy and (1) the incidence of poliomyelitis and (2) the development of bulbar poliomyelitis, as well as in an attempt to determine whether tonsillectomies and adenoidectomies should be discontinued during the summer months of highest incidence of poliomyelitis, Miller surveyed a series of 1,229 cases of poliomyelitis occurring in Los Angeles County during the epidemic year 1949.

The results of the statistical analysis indicate no clinical or significant statistical deviation between the actual and the expected incidence of poliomyelitis developing in Los Angeles County during 1949 in patients recently tonsillectomized and adenoidectomized, even from July through October. In view of these observations, Miller believes there is no reason to discontinue the performance of indicated tonsillectomies and adenoidectomies during the summer months.

ALPERS, Philadelphia.

Poliomyelitis: Infectious or Metabolic? W. J. McCormick, Arch. Pediat. 67:56 (Feb.) 1950.

Paralytic disease could be produced in monkeys by intracerebral inoculation of an extract from the central nervous system of a victim of poliomyelitis. The disease was therefore, regarded as infectious and communicable, and a filtrable virus was believed to be the causative agent. McCormick noted a similarity between beriberi and poliomyelitis. He has made an extensive study of the comparable features of the two diseases since the 1937 outbreak of poliomyelitis in Toronto. Beriberi has been recognized in the Orient for many centuries. Its incidence in epidemic proportion has become noticeable since the introduction of rice polishing, whereby the vitamin B factors are removed. Likewise, poliomyelitis, although apparently known since ancient

Egyptian times, did not appear in epidemic form until 1840, after the adoption of the patented process of white flour milling, by which the vitamin-B-containing elements are discarded. The bodily requirement of thiamine (vitamin B1) is in direct relation to the metabolic rate. The metabolic rate is higher in childhood and early youth than adulthood; it is higher in the male than in the female, higher in the physically active than in the sedentary and higher in pregnancy. Since the author first advanced the hypothesis of vitamin B deficiency as the basic cause of poliomyelitis in 1937, clinical trial of vitamin B therapy in this disease has been made, with results almost as favorable as in the treatment of beriberi. The dietary history of 200 cases of poliomyelitis revealed a deficiency of thiamine in every case. Frequent references have been made to the influence of surgical operations on the incidence of poliomyelitis. The decisive factor in tonsillectomy or other operations may be that the surgical trauma and anesthesia increase the thiamine requirement. The metabolic concept of poliomyelitis does not exclude the possibility of an infectious process as the initial or febrile stage of the disease; the paralytic involvement may be a sequel to the thiamine depletion brought about by the infectious prelude. Beriberi has been proved to be caused by deficiency of thiamine; yet earlier it was regarded as infectious and contagious, just as poliomyelitis still is regarded. The author calls attention to some unusual features of the recent outbreak of poliomyelitis in the Canadian Artic: the winter incidence, the low hygienic and nutritional status of the Eskimo and the fact that the chief food purchases of some Eskimos at the time of the poliomyelitis outbreak consisted of white flour, white sugar, corn syrup, lard, tea and tobacco, all of which are almost completely devoid of essential vitamins. As another example of the effect of restricted food intake on poliomyelitis incidence, the author cites the 1937 poliomyelitis outbreak in Toronto, at which time the incidence was four times as high among people on relief who had a restricted food intake as among the general population. He regards the associated virus as a biochemical substance produced by the disease, which, although capable of producing paralysis in experimental animals by catalytic chemical action in the nervous system, is not necessarily a means of spread of the disease under ordinary conditions.

J. A. M. A.

Prognosis in Poliomyelitis. R. E. Lenhard, J. Bone & Joint Surg. 32-A:71 (Jan.) 1950.

Lenhard presents a survey of the 1944 poliomyelitis epidemic in Maryland, which was the largest recorded in that state, with 499 cases (24.9 per 100,000 population). There were 16 deaths (3.2 per cent). The survey is a two year follow-up study, and although it represents the probable limit of improvement of muscles, it does not relate the end of the story of deformities. Wherever there is imbalanced power in antagonistic muscle groups, deformities can occur later. It was possible to compare 150 cases in which treatment was by nonsupportive methods with 150 cases in which treatment was by supportive methods. In the former series there were 35 deformities in 22 cases; in the latter, 19 deformities in 15 cases. Thus, fewer deformities occurred in the patients receiving supportive and physical therapy. The results of the 1941 and 1944 epidemics were similar, except that slightly more patients had residual involvement in 1944. Approximately 80 per cent of the patients obtained a good recovery. Treatment should be carefully supervised and guided by muscle examinations. Supportive treatment is important. Delay in recovery and persistence of weakness have been observed in patients allowed to fatigue muscles by overtreatment, 400 much activity or lack of necessary support. Treatment given without regard to the protection of muscles results in more deformities.

Intraspinal and Intrathoracic Tumor with Paraplegia in a Child: Report of a Case. H. J. Svien, Proc. Staff Meet., Mayo Clin. 25:715 (Dec. 20) 1950.

The incidence of tumors of the spinal cord in children is not very great. At the Mayo Clinic during a 10-yr, period only 37 cases were uncovered. The majority of the tumors were gliomas, neurofibromas, sarcomas, and lipomas. No ganglioneuromas were found. The hourglass type of tumor makes up only a small fraction of all tumors of the spinal cord (5 of the 37 cases of the present series).

A large variety of tumors occur in the mediastinum. The commonest tumor in the posterior mediastinum is of nerve origin. The hourglass, or dumbbell, tumors of the mediastinum are almost always of nerve origin.

Svien describes a 5½-year-old child who, after developing normally to the age of 1½ yr., had progressive difficulty in walking until there were total paralysis of the lower extremities and incontinence of the bladder and bowel. Examination showed absence of abdominal reflexes and the Babinski sign and ankle clonus bilaterally. Roentgenograms revealed a paravertebral mass from the seventh to the 11th thoracic vertebra. A diagnosis of intraspinal and intrathoracic tumor was made.

A bilateral thoracic laminectomy from the seventh through the 12th vertebra was done. This exposed a large encapsulated extradural tumor lying in the full extent of the laminectomy area. It could be seen that the tumor entered the spinal canal from the chest through the enlarged foramen between the ninth and 10th thoracic vertebrae. The intraspinal portion of the tumor was removed. Microscopic examination revealed a ganglioneuroma, relatively benign. The patient moved her legs on the fifth postoperative day and was able to void normally when the urethral catheter was removed on the eighth day.

Two weeks after the first operation the intrathoracic mass was removed. The main body of the tumor involved the sympathetic chain, the splanchnic nerves, and the three or four inter-

costal nerves which lay deep or external to it.

The patient's convalescence was uncomplicated, and, when discharged 29 days after the operation on the spinal cord, she was able to walk without assistance. When she was reexamined four months later, there was no suggestion of recurrence. The only finding of note was some degree of scoliosis. Because of the favorable histologic diagnosis and the patient's satisfactory progress, the outlook was considered hopeful.

Alpers, Philadelphia.

Tumors of the Spinal Cord Without Neurologic Manifestations, Producing Low Back and Sciatic Pain. H. W. Dodge Jr., H. J. Svien, J. D. Camp and W. McK. Craig, Proc. Staff Meet., Mayo Clin. 26:88 (Feb. 28) 1951.

Attention is called to the possibility that in a few patients with low back pain and sciatica who have no sensory, motor, reflex or sphincter disturbances and who present a typical history of herniated disk tumor of the spinal cord may be the causative agent. During a two year period, 1,242 patients were operated on for removal of herniated lumbar disk. During the same period the diagnosis of "suspected protruded disk" was made, on the basis of the initial general orthopedic, neurologic and roentgenographic examinations, in an additional 27 patients, who were found actually to have tumors of the spinal cord. Of this group of 27 patients, 12 had no sensory, motor, reflex or sphincter disturbance. Attention is called to the high location of most of these lesions, some occurring far above the low lumbar location usually associated with the low back and sciatic pain resulting from a herniated lumbar intervertebral disk.

Neurofibromas and meningiomas make up a greater part of the intraspinal tumors which produce pain and disability. However, tumors of the glioma group and ependymomas may occur.

In all persons who complain of low back and sciatic pain without evidence of any change in the routine roentgenograms or in the neurologic examination an intraspinal tumor should be suspected. For such persons, spinal puncture should be done for examination of the cerebrospinal fluid, and myelograms should be made, so that the possibility of an intraspinal tumor may be ruled out as the causative factor in the production of low back and sciatic pain.

ALPERS, Philadelphia.

Peripheral and Cranial Nerves

PARALYSIS FROM TETANUS ANTITOXIN. L. B. DAVIS, J. Nerv. & Ment. Dis. 113:61 (Jan.) 1951.

In a white youth aged 18, who was free from ordinary allergies and who showed no unusual response to intradermal testing, serum sickness developed one week after an injection of tetanus antitoxin. He experienced persistent pain in the right shoulder, and there soon developed weakness of the scapular and shoulder muscles supplied by the fifth and sixth cervical nerves. Three months after the onset there was pronounced atrophy of the affected muscles. Complete recovery followed eight months of treatment with vitamin B therapy and physical therapy.

BERLIN, Chicago.

FACIALGIA (ATYPICAL FACIAL NEURALGIA): REPORT OF CASES ASSOCIATED WITH TIC DOU-LEUREUX. A. A. RANEY, R. B. RANEY and C. R. HUNTER, J. Nerv. & Ment. Dis. 113:223 (March) 1951.

The authors report four cases of tic douleureux associated with atypical facial pain. The latter was characterized by diffuse deep aching pain in the face that was difficult to localize and of such intensity that the patients were unable to tolerate it. All the patients were relieved of their trigeminal neuralgia by tractotomy or neurectomy but complained of the facial pains. Some experienced associated suboccipital pain and pain in the arm and neck. Roentgenograms showed narrowed intervertebral spaces and spur formation, which, with the subjective findings, were interpreted as indicating disk disease. The authors believe that the postoperative residual pains were due to the changes in the cervical disks.

Berlin, Chicago.

SEVERE DIABETIC NEUROPATHY WITH RIGHT PHRENIC NERVE PALSY. E. MONTUSCHI and G. MELTON, Proc. Roy. Soc. Med. 41:101 (Feb.) 1948.

Montuschi and Melton report the case of a white man aged 57 who had had diabetes for four years. When first seen he complained of cramps in his legs, weakness of the legs and right arm and dimness of vision. Examination revealed diabetic neuroretinitis bilaterally, Argyll Robertson pupils and severe polyradiculitis, including paralysis of the right side of the diaphragm. The cerebrospinal fluid protein was 325 mg. per 100 cc.; there were no cells, and other laboratory tests revealed a normal condition except for the moderately severe diabetes, which was controlled with insulin. The cardiovascular system was normal, and there was no evidence of syphilis.

BERRY, Philadelphia.

Acute Leukemia with Polyneuritic Syndrome and Leukemic Infiltration of Nerves.

T. Alajouanine, R. Thurel, P. Castaigne and F. Lhermitte, Rev. neurol. 81:249, 1949.

The authors report the case of a man aged 60, with an ascending polyradiculoneuritic syndrome, characterized by paresthesias and pain and followed in a few days by progressive motor difficulties. Both sensory and motor symptoms ascended in an identical manner. At this point the diagnosis of acute leukemia was made, and death occurred 25 days later, of respiratory paralysis. Histopathologic examination revealed intravascular and perivascular leukemic infiltration in the peripheral nerves, with less involvement of the rest of the nervous system.

The authors discuss the relation of the leukemic infiltrations to the clinical picture and note that haphazardly distributed lesions cannot explain a precisely ascending, symmetrical clinical picture, such as they describe. They also note that severe leukemic infiltrations may occur without clinical signs and that, as in their case, almost the reverse may be true.

LEGAULT, Washington, D. C.

Vegetative and Endocrine Systems

METABOLIC STUDIES WITH ADRENOCORTICOTROPIN IN CUSHING'S SYNDROME AND IN VIRILISM.

L. J. SOFFER, J. L. GABRILOVE and J. W. JAILER, J. Clin. Endocrinol. 10:594 (June) 1950.

Soffer, Gabrilove and Jailer studied the effects of pituitary adrenocorticotropin (ACTH) administered to two women. One of the patients had Cushing's syndrome associated with bilateral adrenal cortex hypetplasia, and the second had a masculinization syndrome with diffuse luteinization of the ovaries. Metabolic studies after the administration of ACTH revealed in both patients an increase in the daily urinary excretion of 17-ketosteroids and 11-oxygenated steroids and leukocytosis in the peripheral blood, associated with a reduction in the absolute number of cosinophils. The patient with Cushing's syndrome showed a striking decrease in the urinary excretion of sodium and chloride with no change in the urinary excretion of potassium. Calcium was excreted in excess of the calcium intake; phosphorus was also excreted in large amounts. The patient with the virilization syndrome showed no alteration in the urinary excretion of sodium and chloride, a slight potassium diuresis and only a slight increase in the excretion of calcium and phosphorus.

Frankel, Philadelphia.

Association of Congenital Spastic Quadriplegia and Androgenic Precocity in Four Patients. W. H. Perloff and J. H. Nodine, J. Clin. Endocrinol. 10:721 (July) 1950.

Perloff and Nodine report on four children with congenital spastic quadriplegia associated with the premature development of pubic hair and elevated urinary 17-ketosteroid excretion. The manifestations of androgenic stimulation is thought to be the result of precocious adrenarche, which occurs because of agenesis or destruction of a center in the brain located in or near the posterior hypothalamus, the function of which is to prevent pituitary stimulation of the androgenic zone of the adrenal until the time of puberty.

Frankel, Philadelphia.

METABOLIC CONSEQUENCES OF SPINAL CORD INJURY. I. S. COOPER, E. H. RYNEARSON, C. S. MACCARTY and M. H. POWER, J. Clin. Endocrinol. 10:858 (Aug.) 1950.

Cooper, Rynearson, MacCarty and Power studied 16 adult men who had experienced trauma to the spinal cord. During the acute post-traumatic period the men who had undergone severe injury to the spinal cord demonstrated urinary excretion of large amounts of nitrogen, creatinuria and impaired liver function. During the postacute and chronic periods, the course of some of these patients was marked by lowered excretion of 17-ketosteroids and corticosteroids, gynecomastia, testicular atrophy, decreased metabolic rate and hypoproteinemia. Each patient had one or more of these symptoms and signs, the complete syndrome being noted in four of the 16 paraplegic patients.

Frankel, Philadelphia.

SIMMONDS' DISEASE: REPORT OF A CASE OBSERVED FOR NINE YEARS, WITH POSTMORTEM FINDINGS. D. L. SEXTON, R. F. MORTON and J. SAXTON, J. Clin. Endocrinol. 10:1417 (Nov.) 1950.

Sexton, Morton and Saxton report on a patient with Simmonds' disease (hypopituitary cachexia) complicated by severe psychologic symptoms. The onset of the illness occurred during her first pregnancy, which was associated with toxemia. Toxemia also occurred with the next two pregnancies. After the third pregnancy the patient became confused and disoriented; she was confined to a psychiatric hospital, from which she was discharged as cured after six months. A year later thorough endocrine study revealed a low basal metabolic rate, hypoglycemia and increased sensitivity to insulin. During the intervening years she had recurrent episodes of weakness, hypoglycemic attacks, depression, negativism and hallucinations.

Postmortem examination revealed atrophy of the thyroid, adrenal glands and ovaries. The pituitary was small; fibrous tissue compressed and distorted the anterior lobe of the pituitary into small groups of cells, which were chiefly chromophobes; there were few eosinophils and no basophils.

Frankel, Philadelphia,

PORPHYRIA OF CENTRAL NERVOUS SYSTEM. D. BRAGE, Semana méd. 56:1091 (Dec. 15) 1949.

Brage says that the course of porphyria with involvement of the central nervous system may be similar to that of a neuroviral infection. The acute attack is due to a latent disorder of the metabolism of porphyria pigments of infectious origin, which becomes active under the effect of certain drugs; the disease is not necessarily hereditary. A woman aged 34 had acute hallucinations and ascending paralysis, of the type caused by a neuroviral infection, shortly after an arsphenamine injection. The cerebrospinal fluid was normal. Porphyrin was found in the blood plasma and in the urine. Blood transfusion and administration of leukotropin aggravated the symptoms and the neurologic signs and increased elimination of porphyrin. The pathologic alterations in the central nervous system were those of depositions of porphyrin in the subcortical zone, microgliar reaction and demyelination. There was vacuolation in the anterior horn cells, Minimal amounts of porphyrin pigments were present in the viscera. The cultures of lisates of the viscera and of body secretions with successive passages gave negative results for a neurovirus infection. There was no history of porphyria in the family.

J. A. M. A.

Treatment, Neurosurgery

MECHANISM OF SUFFOCATION IN SPINOBULBAR POLIOMYELITIS AND EXPERIENCES WITH OPERATIVE TREATMENT. A. SJÖBERG, Arch. Otolaryng. 52:323 (Sept.) 1950.

The symptomatology of bulbar poliomyelitis is dominated by lesions of bulbar cranial nerves, of which 90 to 96 per cent produce dangerous paralyses of the vagus nerve. After a critical analysis of the varying picture of symptoms of bulbar poliomyelitis, it is now agreed in the United States that the alterations lead to hypoxia, with its well known consequences. In the United States, therefore, the prevention of obstruction of the air channels during the treatment is considered essential. Efforts are directed toward preventing the accumulation of carbon dioxide by early tracheotomy and toward postural drainage with suction, control of blood pressure, endoscopic bronchial toilet and the administration of oxygen.

In Stockholm, Sjöberg had 14 patients treated in this way whose condition would hitherto have been considered hopeless, 12 of whom were saved by operative treatment.

The indications for operative treatment coincide with the immediate cause of suffocation, which the author uses as a basis of classification:

- (a) Peripheral respiratory paresis with retention of secretion.
- (b) Aspiration of saliva and vomitus in cases of lesions of the purely bulbar cranial nerve, above all, of paralysis of the vagus nerve.
- (c) Bilateral paralysis of the laryngeal abductors combined with bilateral paresis of the pharynx.
- (d) Spinobulbar lesions manifesting themselves, among other ways, in bilateral paresis of the pharynx, together, in certain cases, with bilateral nuclear paresis of the accessory nerve and injuries to the first and second cervical segments of the spinal cord. The suffocation picture in these cases is dominated by the angle, or rope dent, symptom, which the author describes in detail. The patient runs the risk of being hanged or strangled at any minute by a contraction or tonus excess in his nonparalyzed antagonistic muscles, which draw the hyoid bone backward and upward. If, in addition, a nuclear paresis of the accessory nerve sets in, the rope dent symptom is further accentuated, and the patient's condition is aggravated, owing to a contraction of the nonparalyzed muscles which bend the head backward.
 - (e) Prophylaxis.

In all types of respiratory paresis the respirator treatment may be directly harmful and may even hasten death by suffocation if bronchoscopic suction with or, in exceptional cases, without tracheotomy is not applied immediately.

ALPERS, Philadelphia.

EFFECT OF BILATERAL STELLECTOMY UPON THE CEREBRAL CIRCULATION OF MAN. H. A. SHENKIN, F. CABIESES, and G. VAN DER NOORDT, J. Clin. Invest. 30:90 (Jan.) 1951.

Recent clinical reports on the efficacy of temporary blockade of the stellate ganglia in ameliorating symptoms of cerebral embolism and thrombosis, presumably by relieving collateral vasospasm, have increased interest in the role of the sympathetic system in the intrinsic control of the disturbed cerebral circulation.

Shenkin and his co-workers studied the cerebral circulation of seven patients before and after bilateral stellate ganglicctomy. They found that a significant decrease in cerebrovascular resistance resulted from stellate ganglicctomy. This decrease in cerebrovascular resistance following operation appeared to be greatest in patients with the initially slowest cerebral blood flow and initially most marked increases in cerebrovascular resistance.

ALPERS, Philadelphia.

Muscular System

MYASTHENIA GRAVIS ASSOCIATED WITH HYPERTHYROIDISM: REPORT OF A CASE WITH THYMECTOMY. N. TAYLOR and A. LARGE, Am. J. M. Sc. 221:293 (March) 1951.

A woman aged 44 suffering from exophthalmic goiter, with clinical and laboratory evidence of hyperthyroidism, also complained of severe weakness. The latter responded slightly to neostigmine therapy. Her thyroid disorder improved with propylthiouracil treatment, but the weakness persisted and she was still refractory to neostigmine. A thymectomy was performed, and she was then able to go about her household duties, requiring only small doses of neostigmine. Ultimately, she requires no propylthiouracil.

REPLIA Chicago.

Dystrophia Myotonica, with Special Reference to Endocrine Function (Klinefelter's Syndrome). C. S. Nadler, W. A. Steiger, M. Troncelleti and T. M. Durant, J. Clin. Endocrinol. 10:630 (June) 1950.

Nadler, Steiger, Troncelleti and Durant report on endocrine changes in three cases of dystrophia myotonica, with autopsy in one case. The hormonal assay and microscopic examination of testicular tissue in the male patients presented changes corresponding with a syndrome described by Klinefelter, which is characterized by gynecomastia, aspermatogenesis with aleydigism, increased urinary excretion of gonadotropin, small testes and decreased urinary excretion of 17-ketosteroids. Klinefelter's syndrome was thought to be associated with a primary dysfunction of the seminiferous tubules, the function of the Leydig cells being normal, or only slightly disturbed. Necropsy revealed widespread muscular atrophy; atrophy of the testes, which showed advanced atrophy and hyalinization of the tubules with complete aspermatogenesis; lipid depletion of the adrenal cortex; decrease in the size of the thyroid, and mild hyalinization of the islets of langerhans of the pancreas. The pituitary and parathyroid glands were normal.

Congenital Anomalies

Arnold-Chiari Malformation. A. Richard and P. F. Girard, Rev. neurol. 81:332 (May) 1049

The Arnold-Chiari malformation consists of displacement of the medulla and lower portion of the fourth ventricle and cerebellum into the cervical canal. This is accompanied with distortion of the medulla, lengthening of the lower cranial nerves and protrusion of a tongue of cerebellum through the foramen magnum into the cervical canal. The flow of cerebrospinal fluid is blocked, and hydrocephalus accompanies the condition frequently. Other malformations, such as spina bifida, platybasia and assimilation of the atlas, may, and often do, exist. Complications, such as syringobulbia, cerebellar degeneration and adhesive arachnoiditis, may also exist. The frequent association of spina bifida with the deformity has led to the theory that the downward traction on the contents of the posterior fossa is due to fixation at the site of the dysraphia.

The authors report the case of an 11 year old girl who was admitted for headache, vertigo, stiff neck, papilledema (5 D.), paralysis of the left sixth cranial nerve, labyrinthine difficulties and cerebellar difficulties, particularly in walking. There were no pyramidal signs. Operation and removal of the posterior border of the foramen magnum and opening of the fourth ventricle relieved the intracranial hypertension.

The authors note the following symptoms and signs of the syndrome: (1) intracranial hypertension; (2) signs referable to the lower cranial nerves; (3) signs of compression of the brain stem, most frequently nausea, vomiting and vascular signs, with signs of involvement of the long tracts not frequent, and (4) cerebellar signs.

Roentgenograms reveal only signs of increased intracranial pressure or another accompanying deformity, such as platybasia, which, in turn, may lead to the suspicion of accompanying Arnold-Chiari malformation. Spinal puncture usually reveals block, and injection of iodized oil U. S. P. reveals space-occupying cerebellar tissue high in the cervical canal.

The treatment is surgical and is aimed at relieving the traction and blockage, not at restoring the dislocated tissue to its normal site.

Legault, Washington, D. C.

Society Transactions

PHILADELPHIA NEUROLOGICAL SOCIETY

Helena E. Riggs, M.D., Presiding Regular Meeting, Dec. 1, 1950

Cerebral Cholesteatoma. Dr. WILLIAM W. KAELBER (by invitation).

A review of the literature covering the various aspects of anatomy, development, pathology, diagnosis, and treatment of intracranial cholesteatomas was presented. A new case was reported.

A white woman, aged 68, with an organic psychosis but normal neurological status, was admitted to the surgical service of the Philadelphia General Hospital with extensive decubitus ulcers and died shortly thereafter.

Examination of the brain showed the cisterna magna to be filled with a mass of yellowish white, glistening granules, which were soft, greasy, friable and easily shelled out and which extended into the caudal half of the cerebral aqueduct.

Histologically, the fourth ventricle was found to be lined with an atrophic layer of skin, some of the cells of which contained keratohyaline granules, and in various areas there were seen epithelial pearls, capillary spaces, and a broad band of fibrous and elastic-like tissue characteristic of the dermis. Chemical analysis of the tissue revealed it to be composed of nearly pure cholesterol.

DISCUSSION

Dr. William Whiteley (by invitation): I have had several cholesteatomas in the cerebellopontile angle and one in the frontal lobe, which had no characteristic course apart from that of a tumor of that area.

I recall an interesting case of a cholesteatoma in the cerebellopontile angle in which the condition seemed to be tic douloureux. The woman had had symptoms of trigeminal neuralgia for 20 years and had been treated with alcohol injections, the last one of which was effective for 18 months. She had a cholesteatoma at the angle which was pressing on the fifth nerve and giving her pain.

Dr. Frank Nulsen: I recall a case in the Army in which the cholesteatoma occurred just in front of the chiasmic cistern between the hemispheres, near the genu of the corpus callosum, and had given rise to headaches. The patient had been treated for psychoneurosis for a number of months, and an air study revealed that the lateral ventricles were separated by a mass.

Dr. Frederick Murtagh Jr.: I should like to mention a case in the service of Dr. Michael Scott. A white woman, aged 46, was admitted in June, 1950, with severe headache, nausea, and vomiting of a few weeks' duration. She had bilateral choked disks and exhibited the typical changes of a lesion of the posterior fossa, with acute blocking of the aqueduct. At operation Dr. Scott removed a large pearly tumor from the fourth ventricle. The tissue had the gross appearance and consistency of cooked crab meat. Several almost perfectly formed perles could be seen distributed through the tumor (slide).

Location of Receptors for Tonic Neck Reflexes. Dr. Grayson P. McCouch, Mrs. I. D. Deering (by invitation), Dr. T. H. Ling (by invitation), and Dr. Donald Scott Jr. (by invitation).

The location of the receptive field for the tonic neck reflexes was studied in a series of labyrinthectomized, decerebrate cats. Only the responses to rotation of the neck were studied in the series. Observations on the response to tilting the head, although the number was inadequate, suggested that the conclusions are also applicable to this reflex.

The response was retained unimpaired after section of all muscles connecting the neck or trunk with the head, after bilateral section of muscular and cutaneous branches of the first three cervical nerves, and after resection and denervation of the muscles.

On the other hand, the response was abolished ipsilaterally by unilateral circumcision of the first three cervical roots at their exit from the ligaments and was abolished in all four extremities by bilateral circumcision, although the muscular and cutaneous nerves were left intact. In some animals decerebrate rigidity was lost with the neck reflexes; in others it was unimpaired.

Action potentials were recorded from atlantoaxial and atlanto-occipital ligaments on rotation and on flexion of the head.

It is concluded that the reflex is ipsilateral and that the receptive field lies in the region of the upper joints of the neck,

DISCUSSION

Dr. Grayson McCouch (by invitation): I once precipitated an autopsy on a virtually decerebrate human infant who was born with some malformation in his head by demonstrating these reflexes in him.

Cerebral Apoplexy: A Pathologist's Report to Clinicians. Dr. HELENA E. RIGGGS.

The histories and necropsy studies of 542 patients with acute cerebral apoplexy were reviewed. Focal brain damage in the nature of hemorrhage was present in 227 and encephalomalacia in 315. Neither type of lesion showed any predilection for a specific location. Areas supplied by the ganglionic arteries were most frequently involved; both the pallium and the subcortical ganglia were implicated in 17 per cent. Infratentorial lesions were present in 17 per cent. When intracerebral hemorrhage was present it was associated with intraventricular bleeding in one-half the cases.

The age of 307 patients was under 60. This number comprised 47 per cent of the white and 69 per cent of the Negro patients; 32 per cent of this group showed scars of earlier cerebrovascular lesions.

There was a close association of generalized circulatory insufficiency resulting from organic heart disease, and the occurrence of cerebral apoplexy. Sixty per cent of the series had been under treatment for, or had complained of, manifestations of decompensation prior to the stroke. Signs of circulatory insufficiency or frank decompensation were noted on admission in 60 per cent of the patients. This was confirmed at necropsy. Acute myocardial infarction, hemorrhagic pancreatitis or thrombosis of the aorta or mesenteric vessels occurred coincident with the stroke in 12 per cent of the patients.

CHICAGO NEUROLOGICAL SOCIETY

Joseph A. Luhan, M.D., President, in the Chair Regular Meeting, Jan. 9, 1951

Myoglobinuria with Paralysis (Meyer-Betz Disease): Report of a Case. Dr. Douglas Buchanan and Dr. Paul E. Steiner.

D. W. was admitted to the University of Chicago Clinics on Sept. 25, 1949. He died 12 hours later. He was born on March 30, 1945, after a normal pregnancy. Delivery was without complications at full term. His rate of development was normal, as was that of his younger brother. He had no acute illness until December, 1947. Then, after a few days' illness with an infection of the upper respiratory tract, he was admitted to the Children's Memorial Hospital, Chicago. In the first few days of his illness he had albumin and blood in the urine. Their presence was interpreted as evidence of acute nephritis. Weakness then developed in the left arm and left leg. The deep reflexes were absent in all four limbs, and both plantar responses were flexor. No objective sensory changes were demonstrated. He had nuchal rigidity. A spine sign was present, and Kernig's sign was elicited in both legs. The spinal fluid contained in each millimeter 5 mononuclear cells, 18.6 mg. of protein, and 143 mg. of a reducing substance. The urine was then clear of abnormalities. Four days later he left the hospital with the diagnosis of acute anterior poliomyelitis complicated by transitory acute nephritis. Two months later he was completely well.

On Sept. 22, 1949, there developed an infection of the upper respiratory tract. He coughed but played all day. On September 23 he continued to cough and to play normally. On September 24 he had difficulty in speaking but played normally. On September 25 he arose early. His voice was faint and hoarse, and his eyes were "heavy." He played violently with his father

and then had breakfast. He had difficulty in swallowing and found that his legs were so weak that he could not stand or walk. He did not walk again. When he reached the University of Chicago Clinics, he was very weak but was rational and cooperative. He remained so until his death, 12 hours later. He breathed rapidly, and the movements of his chest were shallow. There was a bilateral partial ptosis, but the conjugate movements of the eyes were full and synchronous in all directions. There was no nystagmus. The pupillary reactions were brisk and normal. The retina and the optic disk were normal in both eyes. Central and panoramic vision was normal. He had no facial weakness; but the palate was completely motionless, and he had great difficulty in swallowing and in speaking. Both legs were completely paralyzed, and both arms were very weak. The deep reflexes were barely present, and both plantar responses were flexor. There were relative hypalgesia and hypesthesia in the peripheral parts of all four limbs. There were head drop and some nuchal rigidity but no spine sign or Kernig sign. The spinal fluid contained 3 mononuclear cells per cubic millimeter. Examination of the peripheral blood showed 14.5 Gm. of hemoglobin, a red cell count of 5,920,000, and a white cell count of 28,000, 92 per cent of which were polymorphonuclear. The carbon dioxide content of the blood serum was 19.4 mm. per liter, the pH 7.36 and the chloride content 94.6 mm. per liter. The urine was Burgundy red in color and contained a few white cells; the specific gravity was 1.020, and the pH, 5.5. A reducing substance was present, and the benzidine test gave a strongly positive reaction. Spectroscopic examination of the urine revealed the pigment present to be myohemoglobin. There was no evidence of porphyrinuria.

The muscular weakness steadily advanced until both arms and the trunk were completely paralyzed. Despite the action of a mechanical respirator, he died. The diagnosis was myohemo-

globinuria with paralysis (Meyer-Betz disease).

A complete autopsy was performed by Dr. Paul Steiner. The spinal cord was normal, and microscopic examination revealed no abnormality of the ganglion cell structure at any level. In the brain, the changes were in the neurons, and microscopic study revealed evidence of a mild toxic encephalopathy.

The urinary bladder and the renal pelvis contained a reddish brown, clear fluid, which was

again proved by spectroscopic examination to contain myohemoglobin.

All the skeletal muscles had evidence of a severe recent progressive degeneration. This change was characterized by a waxy degeneration with vacuolation and necrosis with liquefaction. The degeneration began with clumping of the myofibrils, an accentuation and then separation of the cross striations. The striations then disappeared, and the muscle fibers swelled and became hyalinized, fragmented, and liquefied. The capillaries contained hyaline thrombi, which were formed of fused red cells. There was no inflammatory reaction, and these degenerative changes were not seen in the smooth or the cardiac muscle.

Myohemoglobinuria with paralysis was first described by Meyer-Betz in 1911. There have been 11 subsequent reports in which this diagnosis was made, but the diagnosis was proved by spectroscopic examination of the urine in only one case (Louw, A., and Nielsen, H. E.: Acta med. Scandinav. 117:424, 1944). Three cases with autopsy have been described, but in all three cases death followed some weeks after the onset of the disease. The autopsy reported here is the first to demonstrate the uncomplicated characteristics.

DISCUSSION

Dr. Oscar Sugar: Do you think there is any relation between this disease and the paralysis or other neurological changes which occur with the excretion of porphyrin in the urine?

Dr. Frederick Hiller: In listening to this interesting paper, I was somewhat surprised to hear the name of Meyer-Betz attached to this disease. Meyer-Betz used to be an assistant in the old clinic with which I was associated in Munich, under Friedrich von Müller, and he made a name by conducting on himself a rather heroic experiment. He injected a large quantity of hematoporphyrin into his veins and produced the classic syndrome of acute porphyria. He was sick about half a year and suffered severe lesions of the skin and necrosis of the subcutaneous tissue wherever his skin was exposed to light. We know that this reaction is produced by the photosensitization which occurs in chronic porphyria in human beings.

I am familiar with the syndrome of myohemoglobinuria and its various characteristics. It is a muscular disease, probably toxic, occurring in various circumstances. It seems to be the general experience that patients who recover from Haff's disease do so simply under the effect of local heat applied to the painful muscles. I wonder whether Meyer-Betz is responsible for recognizing myohemoglobinuria as a disease entity, and I would appreciate having the reference to his work on myoglobinuria.

Dr. Douglas Buchanan: Dr. Sugar, there was no evidence of porphyrinuria. Spectroscopic examination of the urine revealed evidence of myohemoglobin.

Dr. Hiller, the original report was by Meyer-Betz (Deutsches Arch. klin. Med. 101:85-127, 1911), and the most recent summary is in Supplement 226, of Acta medica Scandinavica, 1949.

Stimulation Studies on the Insular Cortex of the Monkey. Dr. Theodore B. Rasmussen and Dr. Burton L. Hoffman.

The insular cortex was stimulated electrically in a series of 42 experiments on 35 monkeys under various kinds of anesthesia, including diallylbarbituric acid (dial*), pentobarbital, ether and chloralosane-urethan anesthesia. Such stimulation causes a fall in blood pressure, inhibition of respiration in expiration, decrease in gastric tonus and inhibition of gastric peristalsis. After section of both vagus nerves, the cardiovascular and respiratory effects persist, but the gastric effects no longer occur.

Parameter studies were made by varying the frequency from 1,000 to 5,000 pulses per second, by varying the pulse duration from 0.1 to 20 msec., and by using different wave forms, including the square, sine, rectified sine and exponentially falling types. The type of the response obtained by stimulating the insular cortex in the monkey is not altered by changing these parameters of stimulation.

DISCUSSION

Dr. J. A. Tarkington: On Dr. Hoffman's charts it appeared that the gastric contractions were suspiciously simultaneous with the respiratory fluctuations. I wonder whether these experiments were carried out with the stomach isolated and whether there was any "traction" with the respirations. I notice also that there was no record of respirations along with the bowel recording when both vagus nerves were cut.

Dr. R. Snider: I should like to ask three questions of the authors of this well controlled series of experiments: 1. Did the results vary in animals under light as compared with those under deep anesthesia? 2. Were there any pupillary changes? 3. Was there activity of the extraocular muscles?

Dr. Percival Bailey: It was fortunate for the early investigators that the ordinary alternating current oscillates 60 times a second, since this frequency is optimal for the motor cortex. In order to get responses from other parts of the brain, however, for example, the cerebellum, an entirely different frequency must be used. Therefore, even though in this study very little more was learned by changing the parameters of stimulation, this feature of stimulation experiments should never be forgotten.

The region from which respiratory responses were obtained was all of the type which Bailey and Bonin have called juxtallocortex, with a heavy fifth layer and a ragged second layer.

Dr. Oscar Sugar: I have obtained some difference in results by using different frequencies in stimulating the insular cortex: There was cessation of respiration with the 40 per second frequency, but not with the 4 per second frequency. I was also interested in the anesthesia problem, for in the record shown of the dog with both vagus nerves sectioned there appeared to be no rise in blood pressure after either or both nerves were cut, an occurrence which is distinctly unphysiological. Finally, I wondered whether any experiments were conducted with the animals under artificial respiration, to rule out the effects of respiration on the apparent changes in the gastrointestinal tract.

Dr. Burton L. Hoffman: With regard to Dr. Tarkington's question as to whether the apparent decrease in gastric tonus might not really be secondary to respiratory changes, and actually be produced by the diaphragm, of course, we had considered this aspect of the matter and had satisfied ourselves that the respiratory and gastric effects were entirely independent of each other. If the kymograph records are studied carefully, it is evident that respiratory gyrations are shown in both the record from the bellows on the chest and that from the intra-

gastric balloon. However, during stimulation respiratory gyrations stop in the former without any alteration in the base level of the curve, whereas in the latter, in addition to the dropping out of respiratory gyrations, there is a striking fall in the level of the curve. A comparison of these two curves makes this difference in base level quite apparent.

Various changes in the mechanical setup were made in an attempt to minimize the respiratory effect on the gastric curve. The abdomen was opened wide on occasion, and the balloon was at times introduced through an ileostomy or a gastrostomy opening, as well as from above. By such variation in the experimental conditions the respiratory effect on the gastric curve was minimized.

The most significant evidence that respiratory and gastric effects are entirely separate lies in the observation that the two effects at times had quite different thresholds and could be produced independently. Likewise, when both vagus nerves were cut, the respiratory inhibition was still evident in the kymograph recordings, but no alteration in gastric tone or motility could be demonstrated to occur after insular stimulation. Thus, it is quite clear that the respiratory and gastric effects from stimulation of the insular cortex are quite independent phenomena.

With regard to Dr. Snider's question, I was unable to note any difference in the response regardless of the type of anesthesia used. The effects produced by stimulation of the insular cortex were remarkably consistent at all times. With ether anesthesia the animals were at times allowed to become very lightly anesthetized. Under such conditions the animals would respond as to painful stimuli. They would move violently enough to cause the recording levers to gyrate wildly. We presumed such effects to be the result of painful stimuli arising from stimulation of the Sylvian vessels coursing over the insula.

We did not look for pupillary or extraocular movements, as our attentions were too fully occupied in keeping the various recording systems operating during stimulation.

With regard to Dr. Sugar's question, our work corroborates that of Babkin and Speakman on the dog and cat so far as it is possible to compare the results in the different species. These investigators spoke of stimulating the "insular-orbital" area in the dog and cat. I have not gone further into a consideration of the possible relation of the "insular-orbital" area of dogs and cats to the insular cortex in monkeys.

No particular study was made on the effect of sectioning the vagus nerves. After such section three or four stimulations were made after the blood pressure curve appeared to have become stabilized, and that was the extent of our observations. In the particular case shown here the blood pressure fell after section of each vagus and then gradually leveled off at about the presection level. The effects on blood pressure from stimulation of the insular cortex were then as reproducible as those preceding the section of the vagus nerves.

'We did not place the animals on artificial respiration at any time in order to demonstrate the independence of respiratory and gastric effects. Our methods for showing this have already been discussed in my reply to Dr. Tarkington's question.

Acetylcholine in Neural Function. Dr. RALPH W. GERARD.

Acetylcholine; choline-acetylase, which synthesizes it, and cholinesterase, which leads to its destruction, are widely present in neural and effector tissues. Acetylcholine has been shown to be liberated, with normal function, from a variety of these tissues, and interference with the activity of cholinesterase is, in turn, associated with marked alterations of function. Many theories have consequently been developed which attribute to the formation of acetylcholine, or its release from a precursor, and its subsequent rapid removal by cholinesterase, an important physiological role. It has been assigned the function of transmitter between nerve and autonomic or skeletal muscle effectors, and between neurons in the autonomic and neurons in the central nervous system; and it has been urged as an essential component in the mechanisms of conduction of the nerve impulse in the continuous nerve fiber. Examination of the available evidence leads me to the conclusion that a transmitter role is probable with autonomic effectors, possible in the case of skeletal muscle and the autonomic neural junctions, improbable in the case of the central nervous system, and excluded in the case of nerve fiber conduction. This evidence will be briefly summarized for the cases of the central nervous system and the peripheral nerve.

The main negative evidence in the case of the central nervous system is based on the complete lack of parallelism between the degree of inhibition of the cholinesterase and the

production of neurological symptoms or fatalities, supplemented by the failure of acetylcholine or of drugs acting on the acetylcholine system to produce consistent physiological effects in the central nervous system. Moreover, many of the pharmacological actions of these agents, both central and peripheral, can be shown to be due to effects other than their inhibition of cholinesterase—among other things, they also inhibit a number of the oxidizing enzyme systems. In the case of the peripheral nerve, the negative arguments are based on the distribution of the acetylcholine system, on the physiological inertness of the acetylcholine on direct application, on the fact that cholinesterase can be completely inhibited without disturbance of nerve conduction, and on calculations which show that the total metabolism of nerve could not account for the acetylcholine turnover required. It is suggested, finally, that acetylcholine may be merely one of a group of quaternary substances of which one or another is important in transmission or conduction in different parts of the neural system; or, as an alternate but not mutually exclusive possibility, that the acetylcholine system is important in neural metabolism, but not directly in relation to its role in carrying nerve impulses.

Treatment of Myasthenia Gravis with Octamethyl Pyrophosphoramide (Pestox III):

A Preliminary Report. Dr. J. Alfred Rider, Dr. Sidney Schulman, Dr. Richard Richter, Dr. Hugo C. Moeller, and Dr. Kenneth P. DuBois.

Octamethyl pyrophosphoramide differs from other alkylphosphate anticholinesterase agents in its greater stability and in its exclusively peripheral anticholinesterase action. A trial of this compound in the treatment of eight patients with myasthenia gravis of moderate to extreme grades of severity was reported.

In six of the eight patients it was possible to replace neostigmine completely by octamethyl pyrophosphoramide. In four of these six patients muscular strength was better than that at the height of neostigmine effect, and in two it was at least as good. All six patients preferred octamethyl pyrophosphoramide to neostigmine because of its smooth and sustained action. At the time of the report, five patients had been maintained satisfactorily on the drug for periods of from one to six months.

The two failures were in patients with severe myasthenia gravis in whom the response to neostigmine had been poor. One of these died of respiratory paralysis in a myasthenic crisis which developed during the process of substituting octamethyl pyrophosphoramide for neostigmine. The other had distressingly severe toxic side effects while taking both neostigmine and octamethyl pyrophosphoramide, and the latter was, therefore, discontinued before an optimum dose (as indicated by the blood cholinesterase level) had been attained.

In every case there was a mutual potentiation of toxic side effects when the two drugs were taken together, and this was most pronounced in the two patients with severe myasthenia gravis. In the other patients side effects were mild and were easily controlled with atropine after maintenance on octamethyl pyrophosphoramide alone had been established.

DISCUSSION

Dr. A. John Toman: Rather than comment, I should like to ask two questions. Was there any additional evidence for such a rapid regeneration of neuromuscular cholinesterase as the authors inferred from the return of myasthenic symptoms 24 to 48 hours after octamethyl pyrophosphoramide was withdrawn? Second, I wonder whether the elderly man (case 5) who died after being transferred from octamethyl pyrophosphoramide to neostigmine therapy was given his original full maintenance dose of neostigmine, and thereby overwhelmed. In line with Dr. Gerard's statements, there are many cholinesterases and a variety of actions of particular anticholinesterase drugs, and the observed actions of octamethyl pyrophosphoramide need not all be attributed a priori to an irreversible action on neuromuscular cholinesterase.

Dr. Roland Mackay: It is noteworthy that the substitution of octamethyl pyrophosphoramide for neostigmine in the treatment of many of these patients with myasthenia gravis produced a decided fall in serum cholinesterase level but no clinical improvement. Later, the substitution of neostigmine for octamethyl pyrophosphoramide allowed the serum cholinesterase level to rise without deterioration of the patient's condition. Do these facts indicate that the level of serum cholinesterase bears no relation to the level of that substance at the neuromuscular

end plate, or does it mean that Dr. Gerard has further justification on clinical grounds for his skepticism of the role played by cholinesterase in the transmission of the impulse across the end plate?

DR. RALPH W. GERARD: I was impressed by two points in the evidence which spoke against the theory that the action of octamethyl pyrophosphoramide in myasthenia gravis depends on its inactivation of cholinesterase at the end plates: (1) the clear lack of relation between the low blood cholinesterase level, which continues after use of octamethyl pyrophosphoramide is suspended, and symptomatic relief, which does not, and (2) the failure to control symptoms in one case with octamethyl pyrophosphoramide alone but the success in doing so when the drug was supplemented by a smaller amount of neostigmine. I should ask, therefore, what other evidence the authors have, but have not presented, which leads them to the conclusion that cholinesterase at the end plate regenerates rapidly after octamethyl pyrophosphoramide block-to account for the difference between the duration of symptoms and that of blood esterase effects-rather than the more immediately probable conclusion that the action of octamethyl pyrophosphoramide on the neuromuscular system depends on some factor other than its antiesterase action. I am sure they have such evidence, but I cannot resist pointing out the non sequitur relation between evidence and conclusion as presented. I am reminded of the anthropologist who told a friend that buried copper wires had been discovered in the Western Plains, indicating that the Indians had known telegraphy much earlier than had been believed. His friend replied that this was nothing at all, since he had dug extensively in the Nile Valley and had found no buried copper wires, so that it was clear that the Egyptians had discovered wireless telegraphy.

Dr. Kenneth DuBois: During the clinical use of octamethyl pyrophosphoramide it was possible to measure the cholinesterase activity only of serum and the red blood cells. While measurements of blood cholinesterase may serve as a guide in regulating the dosage during the initial stage of treatment, these determinations must not be interpreted as giving a true indication of the amount of inhibition in skeletal muscle. This is particularly true in the case of octamethyl pyrophosphoramide, because (a) the drug is not evenly distributed throughout the body and (b) our animal experimentation has shown that the rate of reversal of the inhibition of cholinesterase by octamethyl pyrophosphoramide in vivo differs for each tissue.

Dr. Richard Richter: In one sense, the results of treatment of these patients with octamethyl pyrophosphoramide do not seem very impressive. In this small group there were two physiological and three clinical failures, two of them fatal. It would appear from our limited experience that patients whose symptoms are very severe even when they are taking large doses of neostigmine do not do well on octamethyl pyrophosphoramide, that it is difficult, if not impossible, to transfer them from neostigmine to octamethyl pyrophosphoramide, and that it is perhaps dangerous to try to do so. If this proves to be true in general, octamethyl pyrophosphoramide fails to do the most important thing that one might hope for it. On the other hand, all the patients who had been doing more or less well on neostigmine were better satisfied with octamethyl pyrophosphoramide. In some of them strength was better than with neostigmine, and all commented on the smoother and better sustained action of octamethyl pyrophosphoramide throughout the day and night. They were also grateful to be relieved of the inconvenience of the considerable expense of neostigmine therapy. To this extent, at least, octamethyl pyrophosphoramide promises to be a useful agent in the treatment of myasthenia gravis.

Dr. Gerad's criticism of the assumption that acetylcholine and esterase relationships form the entire basis for the myasthenic phenomena is a proper one. Most neurologists using neostigmine have been aware that the answer to the treatment of myasthenia gravis is not always simply to give enough of the antiesterase. Frequently some muscles never respond to the drug, and too often the myasthenic symptoms become completely refractory to huge, often toxic, doses of neostigmine. But I think it is incorrect to say that no correlation has been demonstrated between the esterase levels and the clinical state. None of the patients in this series showed any response to octamethyl pyrophosphoramide until a certain critical depression of the blood esterase levels had been reached, and the degree of the depression was fairly constant for all of them. It would seem that the influence on cholinesterase activity has something, but perhaps not everything, to do with the effect of octamethyl pyrophosphoramide on the muscular weakness of myasthenia gravis.

News and Comment

AMERICAN LEAGUE AGAINST EPILEPSY

The American League Against Epilepsy, at its annual meeting held at Virginia Beach, Va., April 13 and 14, 1951, selected the following officers:

President, Dr. Francis M. Forster, Georgetown University Hospital, Washington, D. C.; vice-presidents, Dr. Benjamin Simon, Ring Sanatorium Hospital, Arlington Heights, Mass., and Dr. John Kershman, Montreal Neurological Institute, Montreal, Canada; secretary-treasurer, Dr. Jerome K. Merlis, Veterans Administration Hospital, Framingham, Mass.; chairman, program committee, Dr. Ephraim Roseman, Louisville General Hospital, Louisville.

The meeting for 1952 will be held at Louisville during the week of April 21.

Obituaries

FREDERIC H. LEWEY, M.D. 1885-1950

Dr. Frederic H. Lewey, professor of neuroanatomy in the Graduate School of Medicine of the University of Pennsylvania, died at his summer home near Pennsburg, Pa., on Oct. 5, 1950. Born in Berlin, Germany, he was the son of an eminent Berlin internist. Dr. Lewey received his medical degrees from the University of Zurich, Switzerland, and Berlin, in 1910. He studied clinical neurology under H. Oppenheim and with R. Cassirer, in Berlin; clinical psychiatry under E. Kraepelin, in Munich; neuroanatomy, under C. von Monakow, in Zurich; neurophysiology, with R. Magnus, in Utrecht, and neuropathology with Nissl, Alzheimer, and Spielmeyer, in Munich. From 1912 to 1914, he was director of the laboratories of the Neuropsychiatric Clinic, the International Brain Institute, at the University of Breslau Medical School. From 1914 to 1919, Dr. Lewey served as a major in the German army during World War I, in France, Russia, and later, in Turkey, where he was in charge of a field hospital. From 1919 to 1930 he was research assistant, then associate professor of medicine at the Second Medical Clinic of the University of Berlin Charité Hospital, with Friedrich Kraus. Until 1934, when he came to this country as a Rockefeller Fellow, Dr. Lewey was secretary of the German Neurological Association. He was assigned by the Rockefeller Institute as a fellow on the neurosurgical service of Dr. Charles H. Frazier, at the Hospital of the University of Pennsylvania, in Philadelphia, with the title of Visiting Professor of Neurophysiology. In 1940 he was made visiting professor of neuropathology in the Graduate School of the University of Pennsylvania School of Medicine, passed his Board requirements in neurology and psychiatry, and became an examiner of the American Board of Psychiatry and Neurology. From 1943 to 1946 Dr. Lewey was a lieutenant colonel in the United States Army Medical Corps and chief of the neurologic service at the Cushing General Hospital. He was also a consultant in neurology to the Surgeon General's Office. In 1947 he was made professor of neuroanatomy in the Graduate School of the University of Pennsylvania School of Medicine and associate professor in neuropathology in the University of Pennsylvania School of Medicine. He was also chief of the peripheral nerve study center at the Hospital of the University of Pennsylvania.

Those of us who were fortunate enough to have been associated with Dr. Lewey, following his arrival in this country in 1934, thoroughly appreciated his complete integrity and vast store of knowledge on subjects neurological, whether clinical, pathological, or investigative. He was a great inspiration to the younger men on the neurosurgical service at the Hospital of the University of Pennsylvania. Dr. Lewey's war service in the Army of the United States was particularly noteworthy, because he insisted that a trained neurologist was an important cog in the wheel of any neurosurgical service. During his tour of duty at the Cushing General Hospital, he became much interested in peripheral nerve injuries and by his guidance and advice did much to make that center one of great significance in the study and proper treatment of wounds involving peripheral nerves. The establishment of peripheral nerve

study centers throughout the country, to aid in adequate after-care and valuable follow-up studies on these wounded men, was due in great measure to Dr. Lewey's vision and constant advice to the authorities in Washington.

It was a great privilege to have known Dr. Lewey and to have been closely associated with him. He was an internationalist, with an amazing firsthand knowledge of all the well-known neurologists and neuropathologists in Europe, having



FREDERIC H. LEWEY, M.D. 1885-1950

keen judgment of their abilities and a very wide acquaintance with all their publications. To have had the opportunity to study under Dr. Lewey and to observe the meticulous and thorough fashion in which he conducted a neurologic examination was excellent training for all of us, young and old, on the neurosurgical service. We shall miss his kind heart, his clear head and his uncanny skill in solving difficult problems in neurologic diagnosis.

Book Reviews

The Yearbook of Psychoanalysis, 1950. Volume VI. Edited by Sandor Lorand, M.D. Price, \$7.50. Pp. 307. International Universities Press, Inc., 227 W. 13th St., New York 11, 1950.

The sixth volume of the "Yearbook of Psychoanalysis" serves an important function by presenting in book form a selection of the most important and stimulating papers in the vast field of current psychoanalytic research. The "Yearbook" has become a book of reference, and, with careful editing, it guides the reader through the many aspects of psychoanalysis. Of special interest in this volume will be the contribution by Robert Fliess, entitled "The Revival of Interest in the Dream." It is followed by four papers dealing with special aspects of dream psychology and covering the most important contributions to this topic in the last years. Anna Freud is represented by her paper "Notes on Aggression"; Annie Reich writes about "The Structure of the Grotesque-Comic Sublimation"; Martin Grotjahn, about "Laughter and Psychoanalysis," and Jones, about "Hamlet's Father."

Die Neurosen und die dynamische Psychologie von Pierre Janet. By Dr. Leonhard Schwartz, with an introduction by Prof. Pierre Janet, Paris, and a foreword by Prof. Robert Bing, Basel. Price, 32 Swiss francs. Pp. 465. Benno Schwabe & Co., Klosterberg 27, Basel 10, 1951.

Pierre Janet called Leonhard Schwartz, the author of this volume, his "best qualified pupil." Janet, himself a pupil of the great French psychological school founded by J. M. Charcot, expected Schwartz to continue his work, but Schwartz died shortly after the death of his beloved teacher, and before the publication of this book. This volume is the result of six years' work and is perhaps at best a most detailed description of Janet's dynamic psychology. The emphasis is heavily put on the psychiatric and neurological aspects, owing to the training and background of Schwartz. The interest of the American scholar will probably be limited in this contribution to the history of medical psychology.

The Image and Appearance of the Human Body: Studies in the Constructive Energies of the Psyche. By Paul Schilder, M.D., Ph.D. Price, \$4.50. Pp. 353. International Universities Press, Inc., 227 W. 13th St., New York 11, 1950.

Paul Schilder's classic book, "The Image and Appearance of the Human Body," developed from a short manuscript published in 1923 in Germany under the title "Koerperschema." In this short but pertinent study Schilder shows those mechanisms of the central nervous system which are of importance for the development of the spacial image which everyone has about himself. He enlarged the original in later years and published in 1935 a book of which the present publication is a new edition. Schilder develops a new theory which incorporates in a psychological doctrine life and personality as a unit. He uses the insight psychoanalysis has given for the elucidation of problems of brain pathology. The book is based on empirical investigation concerning the image of the human body and in this way deals with one of the

central problems of psychology. The new publication of this book is a great service to the students of medical psychology.

Emotions and Clinical Medicine. By Stanley Cobb, M.D., with introduction by John R. Reid, Ph.D. Price, \$3.00. Pp. 243. W. W. Norton & Company, Inc., 101 5th Ave., New York 3, 1950.

The first half of the book deals with the "physiology and anatomy" of emotion, especially with regard to the hypothalamus, endocrinology and the autonomic nervous system. The second half contains the clinical application to various problems of psychosomatic medicine. The introduction by John R. Reid is a delight for the crusader against semantic confusion in the field.

Sex Offenses: The Problem, Causes and Prevention. By Manfred S. Guttmacher, M.D. Cloth. Price, \$2.50. Pp. 159, no illustrations. W. W. Norton & Company, Inc., 101 5th Ave., New York 3.

This is a timely book on a subject now of great interest, due to a nationwide surge of legislation designed to control sex crime. The author, through his study of actual case material and research into opinions and other expressions on the subject, proposes to clarify questions and attitudes on which most people are very ill informed. The author believes that irrationality and prejudiced thinking are the usual yardsticks by which sexual deviation is measured. He attempts to point out what he feels are the real factors in sex offenses. He attempts to portray cases of actual sex offenders in order to show definite relationships between social, psychological and psychiatric matters as they concern the total problem.

One of the most important factors in this book is the author's discussion of the pathology of deviant sex behavior and the clinical features, based on statistical findings and studies of individual cases. It is felt that this book would be a proper addition to any medical library.

Stuttering. By Charles Van Riper, Ph.D. Pp. 60. Published and distributed by the National Society for Crippled Children and Adults, Inc., 11 South LaSalle St., Chicago, 1949.

This book attempts to achieve a statement concerning stuttering that reflects substantial agreement among professional speech pathologists. Twenty-three well known speech pathologists read the manuscript and offered suggestions as to its content. A rather eclectic point of view of stuttering seems to have been successfully attained by the author. The book disposes of certain popularized, but erroneous, ideas on stuttering.

The principal focus of the book is held on the symptom of stuttering. Very little is said about causative factors or methods for removing them. The fact that stuttering is a symptom exhibited by patients with many neurological and psychiatric disorders is not mentioned. The ontogenetic point of view seems to have been well represented.

That parents usually must do much of the changing to help their children attain normal speech seems to be well agreed. However, methods for bringing about these major changes in interpersonal family and social relationships are not considered. Psychotherapy is not mentioned in the booklet. That relaxation of the patient is one of the cardinal requisites is agreed, but no system or method is considered for accomplishing this skill.

Perhaps the factors listed above, and many others not listed, were an outgrowth of the publisher's limitations placed on the author. Perhaps this booklet, of 60 pages, was about the size prescribed by the publishers. Some important factors on speech correction are well stated by the author in a rather brief way.

Four textbooks on the subject, and one film, are listed at the close of the article.

Neurosis and Human Growth: The Struggle Toward Self-Realization. By Karen Horney, M.D. Price, \$3.75. Pp. 391. W. W. Norton & Company, Inc., 101 5th Ave., New York 3, 1950.

In Karen Horney's opinion, a neurotic process is a special form of human development and constitutes the antithesis of healthy growth. Man's energies are directed toward realization of his own potentialities. Under traumatic conditions, a person may become alienated from his real self and then misdirect his energies into creating and building up a false idealized self based on pride but harassed by doubts, self contempt and self hate. The goal of therapy then would be the liberation of the forces that lead to true self realization. The book is concluded with the following paragraph "Albert Schweitzer uses the term 'optimistic' and 'pessimistic' in the sense of 'world and life affirmation' and 'world and life negation.' Freud's philosophy, in this deep sense, is a pessimistic one. Ours, with all its cognizance of the tragic element in neurosis, is an optimistic one." It is this kind of misinterpretation which distracts the reader from his search for the intrinsic values of Karen Horney's latest work.

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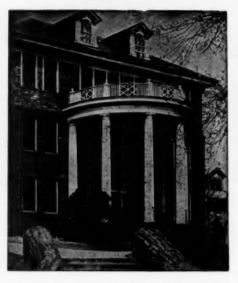
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